3-1-2023 10:00 AM

Speech and Swallowing Outcomes in Patients Treated for Oral Cavity Cancer

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A thesis submitted in partial fulfillment of the requirements for the Master of Science degree in Health and Rehabilitation Sciences

Abstract

This study investigated the natural history of speech and swallowing function of patients treated for oral cavity cancers (OCC) of the oral tongue and/or floor of mouth (FOM), and explored relationships among clinico-demographic and treatment-related variables and speech and swallowing performance. Patient-, disease- and treatment-related data were collected along with clinical outcomes data from medical charts of 72 individuals. Repeated measures analyses revealed changes in speech and swallowing function post-treatment with a general pattern of worse function at hospital discharge and improved function long-term post-treatment, although function did not return to baseline levels. Correlation and regression analyses identified that, in combination, an individual's comorbidity status, tumour staging, and adjuvant treatment can predict variance in the normalcy of one's diet and the social aspects of eating post-treatment. These results have the potential to inform patient education and counselling regarding anticipated outcomes and enhance future treatment decisions.

Keywords: oral cavity cancer, speech, swallowing, dysphagia, quality of life, older adults, comorbidity

Summary for Lay Audience

Head and neck cancers (HNC) are diseases that occur within the oral cavity (mouth), pharynx (throat) and larynx (voice box). Cancers of the oral cavity, specifically those affecting the tongue and floor of mouth (FOM), impact speech and swallowing function, and quality of life (QOL), or one's overall state of well-being. Given the high risk of functional impairment following oral cavity cancer (OCC) surgery, this investigation looked at the speech and swallowing function of patients treated for OCCs of the tongue and/or FOM. Further, this study examined relationships among patient-, disease-, and treatment-related variables (e.g., age at diagnosis, sex, co-existing conditions, etc.) and speech and swallowing performance, in order to identify potential predictors of function.

From the medical charts of 72 patients with OCC, we collected information related to the patient, their cancer, and the treatment they received. In general, changes in speech and swallowing function occur immediately after surgery, and while these functions improve in the long-term (6- to 12-months post-treatment), function often does not return to normal. Interestingly, patients rated their swallowing-related QOL the same at one-year after treatment when compared to before treatment. Age was found to be related to swallowing-related QOL, suggesting that older individuals report their swallowing difficulty has less of an impact on their daily activities than younger individuals. Also, treatment-related characteristics such as the use of adjuvant treatment (additional treatment given after primary surgery) was related to poorer speech and swallowing function.

These preliminary results have the potential to help the clinical team counsel patients regarding anticipated speech and swallowing outcomes. However, to better understand why

some patients experience better speech and swallowing outcomes than other patients, the search for other meaningful predictors of outcome in this patient population should continue.

Acknowledgements

I would like to acknowledge and give my warmest thanks to my thesis supervisor, Dr. Julie Theurer, who made this work possible. Her continued advice, encouragement and guidance supported me through all the stages of writing this project. Simply put, without her insight and knowledge, this project would not be what it is. Thank you for also giving me the opportunity to gain invaluable skills and friendships, it has been an absolute privilege.

I would also like to give special thanks to Martin and my family as a whole for their continuous support and understanding when undertaking my research and writing my project. I am extremely grateful for your continued belief and unconditional support in me, both of which have contributed to my success.

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Chapter 1

1 Introduction and Literature Review

1.1 Overview

Head and neck cancers (HNC) are malignancies that arise in the regions of the nose, mouth, and throat. HNCs, and the medical treatments used to achieve cure for these cancers, lead to significant challenges for survivors, not the least of which include altered speaking, eating and swallowing (Bulbul et al., 2021; Fang & Heckman, 2016; Nguyen, Taw, & Wang, 2018; Suarez-Cunqueiro et al., 2008). The oral cavity is the most frequent anatomical site of HNCs, with approximately 37.3% of cases arising from this region (Gilyoma et al., 2015), and not surprisingly, patients with oral cavity cancer (OCC) are at risk for poor functional outcomes. Speech and swallowing outcomes strongly depend on the site of the lesion, surgical defect size, tissue reconstruction, and adjuvant therapy (Costa Bandeira et al., 2008; Nicoletti, Soutar, Jackson, Wrench, & Robertson, 2004; Saravanan et al., 2016; Son, Choi & Kim, 2015). In particular, oral cavity lesions affecting the oral tongue and/or floor of mouth (FOM) have been documented as having the greatest impact on oral functioning, often resulting in severe speech and swallowing impairments (Bulbul et al., 2021; Suarez-Cunqueiro et al., 2008). Even prior to treatment, individuals with tongue and/or FOM cancer patients report speech and swallowing difficulties, which are generally exacerbated after surgical resection (Haughey, 1993; Son, Choi & Kim, 2015). In particular, patients with cancer localized to the tongue report reduced speech intelligibility and more articulation errors than patients with cancers of the buccal mucosa, or the intraoral surface of the cheek, both pre- and post-treatment (Saravanan et al., 2016). Similarly, patients with tongue cancers experience greater deficits in eating and swallowing, such as a delay in, and difficulty with, the transport of foods and liquids to the pharynx compared to other oral cavity lesions (Azer & Kshirsagar, 2022; Costa Bandeira et al., 2008; Nicoletti, Soutar, Jackson, Wrench, & Robertson, 2004; Son, Choi & Kim, 2015). OCC survivors may continue to have speech and swallowing deficits well beyond treatment, which is often accompanied by reduced interest in social contact, reduced body image positivity, and consequently, reduced quality of life (QOL; Meyer et al., 2009; Schliephake & Jamil, 2002). While the influence of various oral cancer sites and their treatment on survival is increasingly well understood (Bell et al., 2007; Bulbul et al., 2021; Du et al., 2019; Franco et al., 1993; Pulte & Brenner, 2010; Suarez-Cunqueiro et al., 2008), the factors that influence 'good' versus 'poor' functional and QOL outcomes continue to be explored (Abbas et al., 2019). Accordingly, evaluation of functional outcomes and function-related QOL comprises an important area of focus in the multidisciplinary care of patients with OCC.

The head and neck cancer multidisciplinary team (HN MDT) performs various tasks that uphold best patient care including diagnosing and staging HNCs, selecting best medical management of the cancer in collaboration with the patient, and providing ongoing cancer surveillance and management of treatment side effects (Licitra et al., 2016; Taberna et al., 2020). The health discipline of speech-language pathology participates in the HN MDT, contributing expertise with respect to evaluation and management of speech and swallowing function. Although the involvement of speech-language pathology is deemed essential by provincial and national/international agencies (CCO, 2019; NCCN, 2022), specific care practices have not (yet) been prescribed. As such, speech-language pathology intervention for HNC patients often reflects individual (or institutional) practice patterns. As part of evidence-informed standard care, most speech-language pathologists (S-LPs) incorporate serial evaluation of functional outcomes to document change over time – beginning with baseline assessment before treatment, and periodic evaluation following treatment and through survivorship (the collective experience of being a cancer survivor, including consequences of the disease and its treatment; Miller & Shuman, 2016). In addition to evaluating and monitoring speech and swallowing function and providing management/treatment as appropriate, S-LPs and other HN MDT members provide up-front education and counselling for HNC patients with respect to both disease prognosis and anticipated functional outcomes (Taberna et al., 2020). Further, focus on functional, psychological, and social factors embodies patient-centred care and results in the best management for these cancers (Howren et al., 2012; Jovanovic et al., 2022).

The International Classification of Functioning, Disability, and Health (ICF), a framework developed by the World Health Organization (WHO) in 2001, encourages a broader conceptualization of health and functioning compared to the traditional biomedical model (Centers for Disease Control and Prevention, 2021; WHO, 2001). Through the ICF, health and functioning are considered to be influenced by an individual's health condition (e.g., disorder or disease), their functional state (e.g.., body functions and structures, activities, and participation), and contextual factors (e.g., environmental and personal factors; Bornbaum, Doyle, Skarakis-Doyle, & Theurer, 2013; WHO, 2001). Using the lens of the ICF may permit more full assessment of factors that could influence an individual's outcome following treatment of disease, while simultaneously allowing for collaboration with the patient to ensure their values and preferences are taken into consideration in treatment planning (Jovanovich et al., 2022). In fact, ignoring or dismissing personal factors that may influence a patient's function, can negatively impact an individual's QOL (Brom et al., 2017; Chipidza et al., 2015). In the case of patients with OCC, the ICF supports exploration of disease- and treatment-related variables, as well as demographic attributes such as age, sex, comorbidities, and nutritional health (i.e., body mass index (BMI)) as possible factors that influence functional outcomes. Of these characteristics, age and comorbidities are most likely to instigate a shift away from standard care practices. While advancing age does not appear to be associated with less favourable survival per se (Tomo et al., 2020), it has been demonstrated that elderly patients do not receive the same survival benefit from multimodal treatment compared to younger patients (Oosting & Haddad, 2019). Therefore, the evaluation of functional outcomes in the context of multidisciplinary care should also take contextual factors into account.

The overall aim of this study is to examine speech and swallowing outcomes as documented in multidisciplinary care for patients with OCC. Functional change over time across outcome measures related to speech and swallowing performance will be examined to determine the natural history of speech and swallowing function. Associations between demographic (e.g., age, comorbidity status) and treatment-related variables (e.g., disease severity, reconstruction status) and functional outcomes also will be explored, and attempts will be made to identify potential predictors of functional outcome using clinico-demographic and treatment-related factors. The overall benefits of this type of study include the potential to inform patient education and counselling regarding anticipated outcomes, as well as enhance future treatment decision making in keeping with patient-centred care, while supporting patient pulmonary health, nutrition, communication, and QOL.

This chapter will provide a review of literature related to HNC, and OCC in particular, to characterize the disease and its treatment(s). Then, an overview of speech and swallowing function will be provided, followed by discussion of the impact of OCC treatment on these functions. Finally, potential variables of interest related to patient, disease, and treatment will be described.

1.2 Head and Neck Cancer

HNC is a collective term for malignancies that arise across various anatomic sites of the head and neck (Johnson et al., 2020). HNCs can develop from various cell types, leading to a broad range of cancer histology types including adenocarcinomas (glandular cells), lymphomas (blood cells), sarcomas (bones and soft tissue), and squamous cell carcinomas (epithelial cells; National Cancer Institute, 2021). However, the predominant histology is squamous cell carcinoma (SCC), which accounts for more than 90% of head and neck malignancies (Vigneswaran & Williams, 2015). More specifically, head and neck squamous cell carcinomas (HNSCCs) develop within the mucosal epithelial lining of the oral cavity, oropharynx, larynx, hypopharynx, and the sinonasal tract (Johnson et al., 2020).

HNSCC is the sixth most common type of cancer worldwide (Kawakita & Matsuo, 2017); in 2018, approximately 890,000 new cases of HNSCC occurred and 450,000 deaths were attributed to this disease (Ferlay et al., 2018). Alarmingly, the incidence of HNSCC has been increasing over the past three decades (Pulte & Brenner, 2010) and is anticipated to increase by 30% between 2018 and 2030, resulting in a staggering 1.08 million new cases annually (Johnson et al., 2020). Several risk factors are known to contribute to the development of HNSCC. Tobacco and alcohol consumption are the most common risk factors globally (Johnson et al., 2020); the risk of developing HNSCC increases 35-fold in individuals who use both tobacco and alcohol heavily (Blot et al., 1988; Johnson et al., 2020). Due to the influence of direct exposure either through consumption or inhalation, cancers of the oral cavity are typically associated with tobacco and alcohol use (Jethwa & Khariwala, 2017). However, the rising incidence of HNSCC has been attributed, in part, to an epidemic of virally-mediated cancers related to human papillomavirus (HPV) infection (Elrefaey et al., 2014; Isayeva et al., 2012). In particular, high-risk strains of HPV (such as HPV-16 and HPV-18; see Elrefaey et al., 2014 for further discussion) have proven to be most carcinogenic. Approximately 70% of oropharyngeal cancers are HPV-related (Centers for Disease Control and Prevention, 2021). In comparison to non-virally mediated oropharyngeal cancers, HPV-related tumours respond more favourably to treatment (Johnson et al., 2020). In fact, HPV-related disease is staged differently than HPV-unrelated disease due to the superior prognosis associated with these viral cancers. The prognostic relevance of biologically active HPV infection has been substantiated in oropharyngeal cancer, leading to the use of this information as a relevant risk-stratifying biomarker; no such association has been reported for other HNSCC sites, including the oral cavity (Hübbers & Akgül, 2015). More specifically, the presence/absence of HPV does not appear to have treatment or prognostic implications in cancers of the oral tongue, compared to cancers of the base of tongue (Gonzelez & March, 2022). Yet, despite the increasing incidence of HPV-related tumours, HPV-negative OCCs remain the most common form of HNSCC (Gilyoma et al., 2015).

All HNSCCs are initially staged according to the TNM staging system (AJCC, 2018; Amin et al., 2017; Taibi et al., 2014). This system provides a method for classifying malignancies and assists in prognostic cancer staging (Rosen & Sapra, 2021). The “T” in “TNM” stands for tumour classification, which describes the size of the primary tumour and its invasion into adjacent structures (Rosen & Sapra, 2021). The “N” stands for nodal classification, which describes regional lymph node involvement separate from the primary tumour (Rosen & Sapra, 2021). “M” stands for metastasis classification, which describes the presence of metastases or distant spread of cancerous cells to other organs (Rosen & Sapra, 2021). In general, survival rates are best for early-stage HNSCC and these cancers often require less extensive treatment (Festa, 2021).

Although the survival rate for HNSCCs has improved over the past three decades (Du et al., 2019; Johnson et al., 2020), the overall survival remains at approximately 50%, meaning that half of the people diagnosed with HNSCC succumb to the disease within 5 years of diagnosis (Festa, 2021). By comparison, other common malignancies such as lung, colorectal, breast, and prostate cancers have better 5-year overall survival rates in Canada at 60%, 63%, 90%, and 90%, respectively (American Cancer Society, 2022; American Society of Clinical Oncology, 2021; American Society of Clinical Oncology, 2022; American Cancer Society, 2022). HNSCCs are often diagnosed in advanced stages of disease (with regional and/or distant spread of the cancer), which contributes to poorer prognosis for survival. Indeed, improved survival strongly depends on early diagnosis (Pulte & Brenner, 2010). HNSCC survival is influenced by several factors including anatomical site, age at diagnosis, tumour stage, comorbidities, body mass index (BMI), baseline function, and treatment-related outcomes (i.e., the use of adjuvant therapy; Festa, 2021; Ghanizada et al., 2021; Lee et al., 2016; Saito et al., 2012; Wang et al., 2019; Yip et al., 2010).

Approximately 35% of HNSCC patients become long-term (>4 years post-diagnosis) survivors, and of these survivors, approximately 30% experience severe, often incapacitating, late treatment side effects (Munker et al., 2001). Symptoms vary by anatomic site, yet the most common and bothersome symptoms that develop amongst most HNSCC patients include hoarse voice, throat and tongue pain, trismus (restricted mouth opening), xerostomia (dry mouth), and dysphagia (difficulty swallowing; Alho et al., 2006). Dysphagia is the most common side effect of HNSCC treatment, affecting 60 to 75% of all patients (Govender et al., 2017). Swallowing difficulties can be caused by the tumour itself (by blocking or narrowing the food passage), but they are more commonly experienced as a side effect of treatment (Hutcheson, 2019).

Curative treatment approaches for HNSCC can include surgery or radiotherapy (RT), with the possible addition of chemotherapy. First-line treatment for HNCs is often surgical resection with the goal of achieving oncologic clearance of tumour tissue (i.e., removing the tumour and a margin of uninvolved, healthy tissue) to reduce risk of recurrence (Montero & Patel, 2015; Omura, 2014; Pierik, Leemans, & Brakenhoff, 2021; Ravi & Annavajjula, 2014). Given this guiding principle, surgical resection is superior to other treatment approaches in attaining good local control (i.e., complete removal of cancer cells at the primary site; Shah & Gil, 2008). However, open surgical approaches that are required to access certain HNC subsites (i.e., the oropharynx and the larynx), can result in devastating functional and cosmetic outcomes (Kolokythas, 2010) and have fallen out of favour. In these cases, organ-preserving approaches of RT or chemoradiotherapy (CRT) are preferred, with the goal of preserving function (Garneau, Bakst, & Miles, 2018; Obid, Redlich & Tomeh, 2019).

In order to limit the toxicity burden for patients, one treatment goal is to use as few treatment modalities as possible while maintaining good cure rates. Regardless, most patients receive multi-modal therapy - a combination of these treatment approaches (Alsahafi et al., 2019; Johnson et al., 2020). Not surprisingly, multi-modal therapy increases the risk of negative treatment side effect and late toxicities (Forastiere et al., 2013). For example, standard curative treatment for OCCs is generally surgical resection followed by adjuvant therapy (Montero & Patel, 2015; Omura, 2014; Parmar et al., 2021). Adjuvant therapy, or additional treatment modalities that occur following surgical intervention, may be recommended based on adverse prognostic features of the tumour (Montero & Patel, 2015), to lower the possibility of cancer recurrence. As such, surgical resection of OCCs can result in substantial functional impairments post-treatment (Kolokythas, 2010; Parmar et al., 2021), which may be exacerbated by the effects of RT (i.e., scarring and fibrosis) that can restrict muscle ability and cause strictures (narrowing of the swallowing passage; Hutcheson, 2019).

As such, major functional impairments in speech and, swallowing affect approximately 50% of HNSCC survivors (Rinkel et al., 2016), and are strongly predictive of individuals' quality of life (QOL; Bulbul et al., 2020).

1.3 Oral Cavity Cancer

1.3.1 Epidemiology of OCC

Although the increasing incidence of HNSCCs has been associated with a growing number of HPV-related tumours, OCCs remain the most common tumours, accounting for 37% of HNSCCs (Gilyoma et al., 2015). Each year approximately 400,000 new cases of OCC occur worldwide, with the highest prevalence often recorded in South Asia and Europe (Ferlay et al., 2010). In Canada, the yearly incidence of OCC is approximately 12 cases per 100,000 in men and 5 per 100,000 in women (Laronde et al., 2008). Locally, the London Regional Cancer Program (LRCP) is one of six regional head and neck cancer treatment centres in Ontario and it serves the region of Southwestern Ontario. All patients with HNC in this geographic region receive their cancer diagnosis at the LRCP, and most patients receive centralized treatment at this institution as well. The HN MDT at the LRCP reviews over 400 new cases of HNC each year, and approximately 100 of those patients are diagnosed with OCC (Mundi et al., 2018). Tobacco and alcohol use are the most common etiological risks for OCC in North America, but other behaviours such as betel nut/areca nut chewing and chewing tobacco are more common in the South Pacific (Blot et al., 1988; International Agency for Research on Cancer, 2020; Johnson et al., 2020). OCC is more common among men and usually occurs after the fifth decade of life (Montero & Patel, 2015).

Lesions localized to the oral cavity subsites of the oral tongue and FOM are highly likely to have a significant impact on oral functioning, including severe speech and swallowing impairments (Bulbul et al., 2021; Suarez-Cunqueiro et al., 2008). The tongue is comprised of skeletal muscle, connective tissue, glandular tissue (e.g., mucous and serous secretory glands), and a compartment of adipose tissue, all of which are enclosed in oral mucosal epithelium (Shetty et al., 2019). Some portions of the tongue may be less susceptible to the development of SCC than other subsites. For example, the tongue tip and dorsum (i.e., dorsal surface) have a thick, keratinized epithelium with a high preponderance of taste buds, which acts as a resilient physical barrier for protection against surface abrasions and invasions of pathogens (Gorsky et al., 2004). As such, non-keratinized epithelium (found on the lateral border of the tongue) is a more permeable surface which may lack the ability to resist infiltration of carcinogens (Gorsky et al., 2004). Between 55% and 70% of oral tongue lesions arise on the lateral borders of the oral tongue; SCCs on the dorsum of the tongue are exceedingly rare (3% to 5%; Frazell & Lucas, 1962; Goldenberg et al., 2000; Gorsky et al., 2004). Interestingly, various subsites of the oral cavity contribute more significantly to speech and swallowing function than others, which in turn is associated with the resulting functional impairment (Bhattacharya et al., 2021; Costa Bandeira et al., 2008; Nicoletti, Soutar, Jackson, Wrench, & Robertson, 2004; Sun et al., 2007). For example, the tip of the tongue is significantly involved in the formation of various speech sounds, as its position against the teeth and palate manipulate the speech sound signal (Seikel, Drumright & Hudock, 2020), and its integrity and mobility are also integral to moving food and liquid through the oral cavity during swallowing (Pauloski et al., 1993). Moreover, the lateral region of the tongue bears little functional significance for either speech or swallowing, and as such, lateral tongue resections have the least likelihood of disrupting function (Hara et al., 2003; Theurer & Martin, 2003).

As discussed previously, TNM classification is used to determine overall stage of disease. For OCCs, small tumours (≤2 cm = T1; >2 but ≤4 cm = T2) limited to a single subsite without apparent nodal metastases are considered early-stage cancers (Belcher et al., 2014). Larger tumours of the oral cavity (>4 cm) and/or those invading bony structures are considered advanced-stage cancers, and may or may not be accompanied by nodal metastases (Belcher et al., 2014). Although oral inspection can identify some OCCs early in their progression, the majority are diagnosed in advanced stages of the disease, which portends poorer survival outcomes (Buelvas & Buelvas, 2010; Montero & Patel, 2015). As such, the 5-year overall survival rate for OCCs is approximately 50% (Giraldi et al., 2017).

1.3.2 Curative Treatment for OCCs

The primary goal of treatment is to maximize positive long-term functional outcomes, while minimizing the effects on normal surrounding tissue (Cognetti et al., 2008). This guiding principle influences the standard treatment approaches for various anatomic sites. These surgeries may be offered in combination with neoadjuvant (upfront) or adjuvant chemoradiotherapy (CRT), depending on tumour biology (Gilain et al., 2014; Mendenhall et al., 2009). Since these tumours are easily accessible through the oral aperture, the standard treatment for OCCs is surgical resection (Shah & Gil, 2008). While some early (small) OCCs can be treated with a single mode of treatment, advanced-stage OCCs require multi-modal treatment including large surgical resections and adjuvant (C)RT to control local and regional spread of disease (Day et al., 2003; Johnson et al., 2020). Large resections of the oral cavity lead to significant impairments in oral function (Costa Bandeira et al., 2008; Nicoletti, Soutar, Jackson, Wrench, & Robertson, 2004; Son, Choi & Kim, 2015), but the functional impact can be minimized through reconstruction (closing/filling tissue defects; Alfouzan, 2018). Most early-stage tumours can be locally excised, resulting in a small defect that can be left to heal, or can be closed primarily (i.e., the wound edges are brought and kept together by sutures), with minimal or no impact on function (Sankaranarayanan et al., 2015). Advanced-staged tumours may require composite resections, which involve removal of multiple types of oral cavity tissue (e.g., mucosa, muscle, and/or bone; Ji et al., 2017). In these cases, insertion of additional material (i.e., soft tissue and/or bone) is required for closure of the primary resection (Malone et al., 2004). Without reconstruction, it would be unrealistic to expect speech and swallowing function to be maintained post-treatment (Ji et al., 2017). Still, this combination of surgery and adjuvant therapy comes with higher risk of additional treatment-related toxicities (Day et al., 2003).

1.3.3 Common Post-Treatment Side Effects for OCCs

Surgical resection alters the anatomy of the oral cavity, which has the capacity to negatively impact crucial oral functions (Buelvas et al., 2010; Dzioba et al., 2017). Given that the tongue and FOM are the most commonly affected oral cavity subsites (Gonzalez & March, 2022), it can be expected that the majority of patients with OCC will experience impaired oral function. Tongue resections in particular, have the most potential to impact speaking, eating, and swallowing (Ji et al., 2017). Speech production requires sufficient control of the lips, tongue, and soft palate (Saravanan et al., 2016). The tongue is notably the most important articulator for speech production, as it can be positioned against the teeth and palate to form various speech sounds (Kamrani & Sadiq, 2022; Saravanan et al., 2016; Seikel, Drumright & Hudock, 2020). Impairments in the range of motion, strength and adaptability of the tongue may influence speech production abilities (Saravanan et al., 2016). Dysphagia is among the most frequent long-term side effects of OCC treatment (Son, Choi & Kim, 2015). More specifically, functional swallowing impairment following tongue resection is associated with reduced tongue mobility, reduced muscle structure and mass, damage to the hypoglossal nerve, and postoperative fibrosis and scarring (Ji et al., 2017). In addition to exacerbating functional deficits, adjuvant treatment with (C)RT can induce lesions in the oral mucosa (i.e., oral mucositis) that result in function-limiting pain (Chen, 2019). Other treatment-related toxicities that can influence eating and swallowing include xerostomia, trismus, and fibrosis of muscles within and beyond the oral cavity (Chen, 2019; Logemann et al., 2005). The prevalence of dysphagia is a significant concern because it is associated with serious health consequences such as airway obstruction, aspiration pneumonia, dehydration, and malnutrition (Frontera et al., 2020; Matsuo & Palmer, 2009). The effects of cancer treatment on speech and swallowing will be revisited in greater detail later in this chapter.

While the prevalence and severity of the speech and swallowing impairments typically depends on tumour stage and localization, it seems plausible that other personal factors might influence the prevalence of these functional impairments during and following cancer treatment. In particular, advancing age might predispose patients for functional impairments post-treatment, with the potential to ultimately influence QOL (Costa Bandeira et al., 2008; Nicoletti, Soutar, Jackson, Wrench, & Robertson, 2004; Son, Choi & Kim, 2015). It has been established that, with advancing age, there is a reduction of tissue elasticity, alterations in head and neck anatomy, decreased oral moisture, and sensory impairments, that can influence speech and swallowing function (Azzolino et al., 2019). In turn, negative functional outcomes can also affect one's QOL (Buelvas et al., 2010; Dzioba et al., 2017), and when taken together, the significant impacts on health and QOL highlight the importance of understanding predictors of post-treatment function in attempts to enhance OCC survivors' well-being.

1.4 Speech and Swallowing

The anatomy of oral cavity plays a vital role in speech production, and the initial intake and digestion of food and liquids (Kamrani & Sadiq, 2022; Seikel, Drumright & Hudock, 2020). In particular, the tongue is crucial to speech and swallowing function; the intrinsic muscles of the tongue are primarily involved in changing the shape of the tongue, which is imperative for speech production (Dotiwala & Navdeep, 2022; Kamrani & Sadiq, 2022; Seikel, Drumright & Hudock, 2020). The tongue also enables mechanical digestion through the compression and manipulation of a bolus against the palate (Kamrani & Sadiq, 2022; Seikel, Drumright & Hudock, 2020).

Speech and swallowing are assessed and monitored for all HNC patients, throughout all stages of treatment and recovery (Clarke et al., 2016). Clinical assessments of speech and swallowing include: oral-motor examination (lip closure, range of motion), articulation, tongue control and strength, and speech is usually clinically assessed by perceptual evaluation of voice quality (Clarke et al., 2016). Often patients are also able to report speech and swallowing function through the use of clinician- and patient-reported questionnaires (Cnossen et al., 2012).

1.4.1 Speech Function

Speech production includes the processes of respiration, phonation, articulation, and resonance (Bulbul et al., 2021; McConnel et al., 1998; Seikel, Drumright & Hudock, 2020; Sun et al., 2007). Of these processes, phonation (or voice production), articulation, and resonance are most likely to be affected by the treatment of HNSCCs, with articulation most affected by the treatment of OCC. Phonation is the physiologic process whereby acoustic energy is generated in the larynx by the vibration of the true vocal folds. To achieve voicing, expiratory airflow is constricted by adduction of the vocal folds. Once sufficient subglottal pressure is achieved, the vocal folds are set into vibration. The articulatory process, or the production of speech sounds, involves the active movement of the structures within the vocal tract, such as the tongue and mandible, which give rise to the acoustic elements of speech (Lieberman, 1977; Minifie, Hixon, & Williams, 1973; Hufnagle, Pullonm & Hufnagle, 1978). Finally, the resonant properties of sounds can be altered by manipulating the valve between the pharynx and nasal cavity. The acoustic energy emanating from the vocal folds can be directed through the oral cavity alone using the same mechanism of soft palate elevation that occurs during swallowing. However, to introduce additional resonant properties to specific speech sounds, the soft palate can be lowered and acoustic energy is diverted into both the nasal and oral cavities (Seikel, Drumright & Hudock, 2020).

1.4.1.1 Effects of OCC Treatment on Speech. Speech function is a common concern prioritized by OCC survivors (Clarke et al., 2016). Often, speech challenges first arise early after surgical treatment when patients experience significant needs and concerns but have limited ability to use speech due to acute treatment-related changes (e.g., swelling, pain; Rodriguez & VanCott, 2005). However, it is not uncommon for speech deficits to persist well beyond the immediate post-surgical period and have long-lasting effects on speech intelligibility and communicative effectiveness (Eadie et al., 2013; Rinkel et al., 2016).

Functional speech outcomes are often correlated to the site and size of the resected tissue, TNM staging, and the use of adjuvant therapy (Chen, 2019; Costa Bandeira et al., 2008; Nicoletti, Soutar, Jackson, Wrench, & Robertson, 2004; Son, Choi & Kim, 2015). In general, the degree, extent, and location of surgical resection for OCC treatment determines the resulting speech impairment (Bhattacharya et al., 2021; Costa Bandeira et al., 2008; Sun et al., 2007). For speech specifically, the tongue is one of the most important anatomic structures (Wall et al., 2013). For example, the vowels of a language are identified according to the position of the tongue within the vocal tract, which could be altered as a result of surgical resection (Wall et al., 2013). Preservation of the tip of the tongue contributes significantly to the retention of adequate speech quality; larger resections involving loss of the tip are most disruptive for speech outcomes (Nicoletti, Soutar, Jackson, Wrench, & Robertson, 2004; Sun et al., 2007). Long-term OCC survivors may continue to have both objective and subjective speech deficits up to five-years post-treatment, ultimately affecting QOL (Meyer et al., 2009).

1.4.2 Swallowing Function

Swallowing is a survival mechanism that provides two crucial biological functions: transport of food and fluids through the upper aerodigestive tract and protection of the lower respiratory tract from foreign materials (Matsuo & Palmer, 2009). Swallowing, or deglutition, is an innate function, involving volitional and reflexive activities coordinated across more than 30 nerves and muscles (Logemann et al., 2005; Matsuo & Palmer, 2009). The act of swallowing consists of 4 distinct, but related, phases - the oral preparatory phase, the oral transport phase, the pharyngeal phase and the esophageal phase (Matsuo & Palmer, 2009). In the oral preparatory phase, food is prepared to create a cohesive bolus or a single mass that can be transported quickly and easily (Matsuo & Palmer, 2009). This preparation typically involves chewing (or mastication) to break down solid foods. The duration of this voluntary phase is dependent on the type of material that has been ingested, with food material requiring significantly greater preparation than liquids (Matsuo & Palmer, 2009). As the bolus is prepared, food and liquid is contained in the oral cavity such that this material does not enter the unprotected airway.

Following oral preparation, coordinated action of the tongue results in transport of the bolus from the mouth to the oropharynx – this constitutes the oral transport phase (Matsuo & Palmer, 2009). To accomplish oral transport, the tongue moves in a 'stripping wave' motion in which the dorsal tongue surface moves upward to contact the hard palate and squeezes the bolus backward along the palate. Once the bolus reaches the oropharynx, the reflexive pharyngeal phase is triggered (Matsuo & Palmer, 2009). The pharyngeal phase serves to move the bolus through the pharynx to the esophagus while directing the bolus away from the nasal cavity and airway (Matsuo & Palmer, 2009). First, the entrance to the nasal cavity is closed by elevation of the soft palate and the airway is protected as the larynx closes at several levels and elevates up under the base of the tongue (Matsuo & Palmer, 2009). Then, the muscular walls of the pharynx contract to apply pressure to the bolus while the upper esophageal sphincter opens to permit passage of the bolus into the esophagus (Matsuo & Palmer, 2009). Finally, the esophageal phase results in propulsion of the bolus through the length of the esophagus into the stomach (Matsuo & Palmer, 2009).

The oral preparatory and oral transport phases are most likely to be affected by surgical resection of oral cavity tumours (Bulbul et al., 2021; Logemann et al., 2005). Yet, the disruption to the transition between these voluntary aspects of the swallow and the reflexive pharyngeal phase can also increase the risk of aspiration (material entering the airway prior to the start of the pharyngeal phase; Bulbul et al., 2021; Logemann et al., 2005).

1.4.2.1 Effects of OCC Treatment on Swallowing. Similar to speech deficits experienced by these patients, functional outcomes in eating and swallowing are most often correlated to the site and size of the resected tissue, stage of disease, and the use of additional therapy modalities (i.e., RT; Costa Bandeira et al., 2008; Nicoletti, Soutar, Jackson, Wrench, &

Robertson, 2004; Son, Choi & Kim, 2015). The tip of the tongue and the dorsal tongue are the most crucial subsites of the oral tongue for swallowing. During the oral preparatory phase of swallowing, the tongue tip is raised against the alveolar ridge of the hard palate and the back of the tongue is lowered, breaking the retro-oral seal and creating a path for the bolus to enter the oropharynx (Bulbul et al., 2021; Matsuo & Palmer, 2009). Similarly, during the oral transport phase, the dorsal tongue surface moves upward, expanding the area of the tongue-palate contact, squeezing the bolus backward along the palate and into the pharynx (Bulbul et al., 2021; Matsuo & Palmer, 2009).

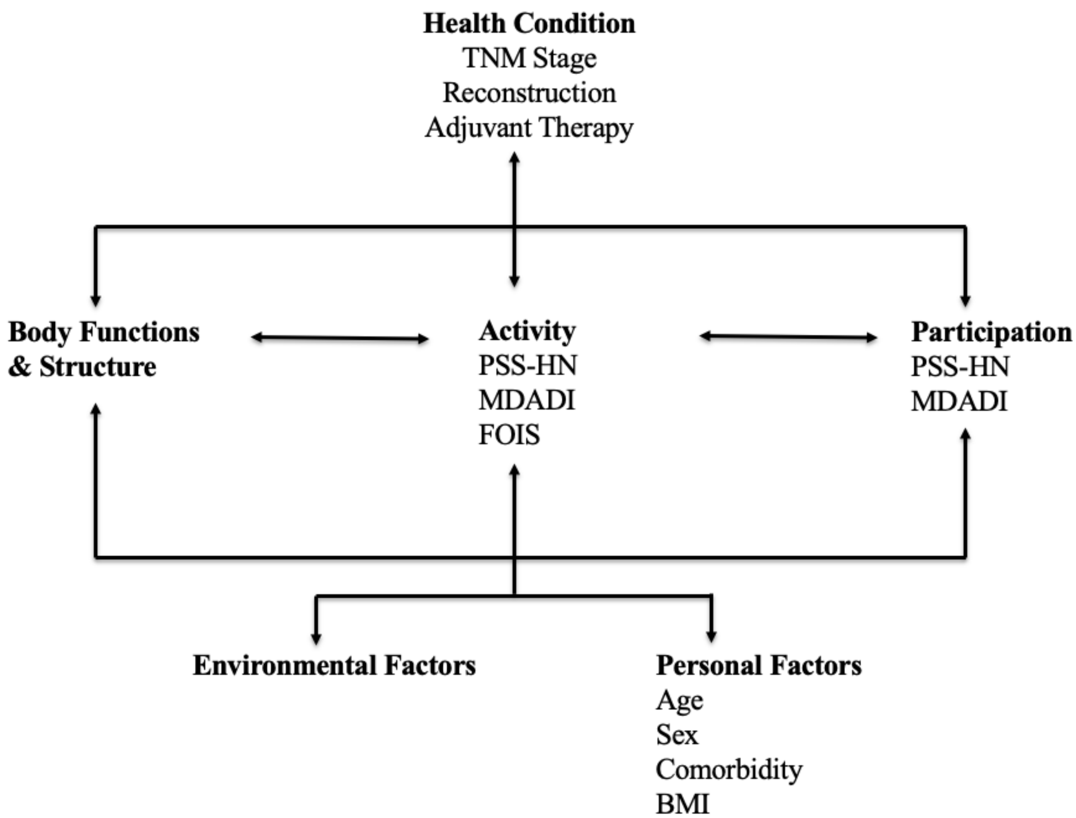
Prolonged chewing and difficulty moving the bolus can result in increased oral transit/transport time, or the length of time required for the bolus to move through the oral cavity (Costa Bandeira et al., 2008; Kweon, Koo, & Jee, 2016). Generally, small resections are associated with better swallowing outcomes (Nicoletti, Soutar, Jackson, Wrench, & Robertson, 2004), while patients with advanced-staged OCC, which result in larger surgical defects, have significantly higher incidence of dysphagia (Costa Bandeira et al., 2008; Ihara et al.,2021). Additionally, patients with larger resections may experience different eating patterns, increased oral symptom frequencies, and more significant psychosocial impacts (Costa Bandeira et al., 2008). As previously mentioned, impairments in speech and swallowing function have the ability to affect one's QOL negatively (Schliephake & Jamil, 2002).

1.5 Variables of Interest

In order to determine the impact of speech and swallowing function on QOL, other variables affecting function should be considered. In particular, oncology patients may benefit from the consideration of personal factors (features of an individual that are "not part of a health condition or health state"; WHO, 2001) when determining risk factors of speech and swallowing impairment, morbidity and to inform decision-making (Bornbaum et al., 2013). The role of clinico-demographic characteristics is of interest, as their influence on oral function post-surgery has been hypothesized (Bornbaum et al., 2013; Colangelo et al., 1996; Day et al., 2003; Fridman et al., 2018; Fujimoto et al., 2007; Gama et al., 2017; Giannitto et al., 2017; Hirota et al., 2020; Jeong et al., 2015; Kamstra et al., 2011; Logemann et al., 2006; Maciejewski et al., 2010; Malone et al., 2004; Siegal, Miller & Jemal, 2016; Ueshima et al., 2021; Zuydam et al., 2005). Some personal factors that might influence function include aspects of the person (age, sex), their overall health (comorbidity, BMI), and their current disease state (site of OCC, tumour stage). It has previously been established that aspects of one's health condition (i.e., tumour stage, reconstruction status, adjuvant therapy status) and their body functions and structure (i.e., tongue strength, tongue base retraction, laryngeal vestibule closure) may influence functional outcomes (Al-Othman et al., 2003; Chen et al., 2019; Logemann et al., 2005; Saravanan et al., 2016; Vincent et al., 2019). Yet the interplay (see Figure 1) between the individual's health condition, their activity and participation, and their contextual factors has not been fully explored. In the following figure, we have mapped our variables of interest in this study onto the ICF framework to demonstrate that multiple viewpoints of health and functioning that will be explored using a retrospective chart review methodology (Figure 1).

Figure 1

Capturing the Variables of Interest through the ICF



Note. Mapping the variables of interest in this investigation to the ICF developed by WHO (2001). Reproduced from International Classification of Functioning, Disability and Health, World Health Organization Geneva, Model of functioning and disability, Page 18, Copyright (2001).

1.5.1 Clinico-Demographic Variables of Interest

1.5.1.1 Age at Diagnosis. Age is a personal factor that may influence postoperative speech and swallowing function in OCC patients (Fujimoto et al., 2007; Haehl et al., 2020). Specifically, there is evidence that temporal speech properties (i.e., articulation rate, articulation rate stability, movement time, etc.) are disrupted with advancing age (Tremblay et al., 2019). Also, the prevalence of dysphagia increases with advancing age, with approximately 10-20% of individuals over the age of 65 experiencing swallowing difficulties (Cichero, 2018; Sura, Madhavan, Carnaby & Crary, 2012).

Diagnosis of OCCs typically occurs in individuals aged 60 years of age or older (Chitapanarux et al., 2006). In fact, only 5% of cases occur in patients aged 40 or younger (Veness et al., 2003). Moreover, overall survival is significantly better among these younger patients as they tend to have less advanced disease and are less likely to have smoking-related cancers (Yip et al., 2010). With respect to cancer treatment, advancing age may influence treatment selection (Haehl et al., 2020), but when comorbidities are accounted for, advancing age does not appear to be associated with less favourable survival (Tomo et al., 2020). Interestingly, the impact of advancing age on functional outcomes and QOL following both HNSCC, in general, and OCC treatment has not been well-studied. A few studies have reported a negative relationship between age and speech and swallowing function following treatment for OCC (Fujimoto et al., 2007; Hirota et al., 2020; Tremblay et al., 2019), while others have not substantiated these results (Sarini et al., 2001; Worley et al., 2018).In light of the documented age-related changes in speech and swallowing, it is of interest to investigate whether age is an important prognostic factor for function following treatment of HNSCC, and particularly in OCC given the advanced age of diagnosis for many of these cancers.

1.5.1.2 Comorbidities. In addition to age, comorbid conditions significantly influence outcomes following OCC resection (Lee et al., 2016). More specifically, worse disease-specific survival and poorer oral functional outcomes are associated with greater comorbidity burden (Lee et al., 2016). As such, evaluation of comorbid conditions may also be useful in identifying individuals at greater risk for functional impairment. The Charlson Comorbidity Index (CCI) is one tool that can grade severity of comorbidities using information gathered from medical records (Charlson et al., 1987).

Within the literature, hypertension and chronic obstructive pulmonary disease have emerged as the most prominent comorbid conditions that occur with advancing age (Yancik et al., 1998). Multiple comorbidities at diagnosis have the potential to increase the complexity of cancer management, and also affect survival outcomes (i.e., increased risk of early mortality; Yancik et al., 1998). In studies that examined that relationship between age and function in OCCs, the presence of comorbidities was not assessed (Fujimoto et al., 2007; Hirota et al., 2020; Tremblay et al., 2019).

1.5.1.3 BMI. Baseline BMI can act as a nutritional marker and may provide surrogate information related to an individual's eating and swallowing function. While high BMI (i.e., obesity) may contribute to higher recurrence rates and poorer survival prognoses (Iyengar et al., 2014; Wang et al., 2019), patients with low BMI may have a greater risk of negative post-treatment consequences (Saito et al., 2012; Wang et al., 2019). High BMI can also be associated with an increase in muscle mass; this may translate into positive post-treatment outcomes with protection against the negative effects of sarcopenia (or, loss of skeletal muscle mass) after OCC treatment (Hicks et al., 2018).

1.5.1.4 Sex. The current body of literature recognizes that there are different distribution patterns of clinico-demographic and pathological factors when comparing women to men in OCC patients (Bonifazi et al., 2011; Garavello et al., 2008; Girod et al., 2009). In tongue cancers specifically, it has been revealed that tongue strength diminishes more in women than it does in men post-operatively (Youmans, Youmans, & Stierwalt, 2009). The health differences between sexes has been explained by varying exposure to social factors throughout life, which can ultimately lead to different health outcomes (Zunzunegui et al., 2009). Yet, the impact of biological sex on function is not well understood and is of interest within this study.

1.5.1.5 Disease Stage. Patients with early-stage tongue and/or FOM cancers tend to demonstrate better survival and functional outcomes, in comparison to those with advanced disease (Almangush et al., 2021). As such, disease staging is a factor that requires consideration. From a cancer control perspective, surgical resection of early-staged tumours may provide sufficient disease control, without the need for additional treatment. However, in cases of positive or close surgical margins, where cancer cells are identified in or near the edge of the resection specimen (Alicandri-Ciufelli et al., 2013; Hamman et al., 2022), or with evidence of disease spread to adjacent lymph nodes, adjuvant therapy may be recommended (Fridman et al., 2018).

1.5.2 Treatment-Related Variables of Interest

In addition to these clinico-demographic factors, treatment-related factors, such as reconstruction, adjuvant therapy, and the use of feeding tubes (FTs) may influence postoperative speech and/or swallowing function in patients with oral cavity cancer (Al-Othman et al., 2003; Chen et al., 2019; Logemann et al., 2005; Saravanan et al., 2016; Vincent et al., 2019).

1.5.2.1 Reconstruction. In light of their relative importance for oral function, reconstruction of surgical defects of the tongue and FOM is often crucial for patient functioning and well-being post-surgery (Haughey, 1993). The primary goal of reconstruction is to restore structures such that speech and swallowing function can approximate the patient's "normal" pre-cancer level of functioning (Saravanan et al., 2016; Vincent et al., 2019).

For large defects, reconstruction using pedicled flaps or free-flaps (i.e., tissue transfer) have allowed for better speech, swallowing, and QOL outcomes in most patients (Riva et al., 2022; Vincent et al., 2019). In particular, free-flap reconstruction has demonstrated numerous benefits for these patients including intelligible speech production, resumption of an oral diet without the need for a permanent FT, and QOL at one-year that is similar to baseline QOL (Vincent et al., 2019). Regardless of surgical attempts to improve oral function, swallowing challenges that limit an individual's ability to meet their nutritional needs are common.

1.5.2.2 Adjuvant Therapy. The use of adjuvant therapy exacerbates these challenges and affects the severity of functional outcome (Chen et al., 2019; Logemann et al., 2005); Shin et al., 2012). Specifically, adjuvant therapy following resection negatively affects speech and swallowing function, compared to surgery only (Shin et al., 2012). This may be explained by the excessive shrinkage of tongue tissue following RT, resulting in a decrease tongue coordination (Shin et al., 2012). As previously mentioned, in addition to the treatment itself, RT may also induce late complications, such as xerostomia, oral mucositis, trismus, and fibrosis of muscles beyond the oral cavity (Chen et al., 2019; Logemann et al., 2005; Shin et al., 2012). In fact, in patients receiving adjuvant therapy, enteral feeding support often is required to ensure the nutritional needs are met (Nugent et al., 2013). Given the established relationship between adjuvant therapy and functional decline, it is of interest to control for the impact of adjuvant therapy on speech and swallowing function in this investigation.

1.5.2.3 Enteral Feeding. The current literature outlines the concern of FT placement, as it often is accompanied by a subsequent reduction in oral intake (Al-Othman et al., 2003). In particular, FT placement may result in atrophy (wasting or loss of muscle tissue) of the important structures involved in swallowing and increase the probability of long-term FT dependence (Al-Othman et al., 2003). Generally, patients who use FTs for long periods of time are at a higher risk of severe dysphagia (Petersson, Finizia, & Tuomi, 2021; Quon et al., 2015). It is possible that the length of FT use is a predictive factor of speech and swallowing function postoperatively in OCC patients (Murphy, Ridner, Wells, & Dietrich, 2007; Petersson, Finizia, & Tuomi, 2021; Quon et al., 2015).

1.5.3 Issues Arising from the Literature

Given that previous research suggests that baseline and treatment-related characteristics impact function, the relationship between these characteristics and functional outcomes in patients treated for tongue and/or FOM cancers is worthy of further investigation. In previous studies on functional outcomes after surgery as treatment, predictors of speech and swallowing function included, but were not limited to, baseline function, t-stage, n-stage, and adjuvant treatment (Hsiang et al., 2019; Pierre et al., 2014). Although age wasn't necessarily the focus of these studies, some authors suggest that age might be another independent risk factor that influences swallowing function (Fujimoto et al., 2007; Hirota et al., 2020; Tremblay et al., 2019). A few studies have reported a negative relationship between age and speech and swallowing function following treatment for OCC (Fujimoto et al., 2007; Hirota et al., 2020; Tremblay et al., 2019), while others have not substantiated these results (Sarini et al., 2001; Worley et al., 2018).

Therefore, one of the objectives of the current study is to explore the relationships between age and speech and swallowing function.

Moreover, the existing literature that has investigated age as a potential predictor of speech and swallowing function contains several methodological challenges. Firstly, age, as an independent variable, has been defined inconsistently across studies with little consensus on methods for delineating ‘young’ individuals from ‘old’ individuals (Gugić & Strojan, 2013; Sarini et al., 2001). As a result, various age brackets or cut-off values have been used to define ‘older age’ across publications. For example, “old” has been defined as 60 years of age and older and “oldest age” as 85 years of age and older (Jardine et al., 2020). Yet, in other publications, the age of 65 has been considered “young old”, 75 years as “old old” and 85 years as the “oldest old” (Jardine et al., 2018). Additionally, research on the impact of age as a predictor of outcomes often group cancers of the oral cavity and oropharynx together (Chen, 2019; Vandersteen et al., 2013). This should be avoided as these cancers are different biologically, and are treated very differently, making it difficult to tease apart the effects of age, disease, and treatment. .

Secondly, the personal factor of age is most often defined using chronological age, or age in years since birth (Guralnik & Melzer, 2002). Yet, some valuation of the presence of comorbid health conditions that influence how active or healthy an individual is relative to their age-matched peers, may provide a more sensitive measure of age-related factors that influence survival and function compared to chronological age per se (Gugić & Strojan, 2013).

A third, and final, issue with the current literature examining outcomes following OCC treatment is that some of the relationships being reported between the independent variables of interest and speech and swallowing function did not use function-specific outcome measures. Instead, researchers used individual items from general QOL outcome measures, such as the

Quality of Life Questionnaire - Head and Neck Module (QLQ-H&N35) and the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC-QLQ) in order to determine relationships with speech and swallowing (Vandersteen et al., 2013). This study aims to investigate the change in speech and swallowing function with the use of function-specific outcome measures. Speech function was assessed using the Performance Status Scale – Head and Neck (PSS-HN; Speech) subscale. Similarly, swallowing function was assessed using the PSS-HN (Diet and Eat) subscales, the Functional Oral Intake Scale (FOIS), and the M.D. Anderson Dysphagia Inventory (MDADI).

1.6 Rationale for the Current Study

As mentioned above, several clinico-demographic and treatment-related variables are known to be predictors of health outcomes, yet study of the impact of personal factors on functional outcomes is lacking. In particular, age is emerging as a variable of interest in patients with OCC. Dysphagia and older age are believed to be related, as older adults are more susceptible to dysphagia and its consequences (Lui & Nguyen, 2018; Saposnik et al., 2008; Muhle, Wirth, Glahn & Dziewas, 2015; Sura, Madhavan, Carnaby & Crary, 2012). However, methodological issues (e.g., lack of consensus and operational definitions for 'older age') in the current literature limit our understanding of the relationship between this personal factor and treatment outcomes.

Therefore, the primary aim of this study is to investigate potential relationships between the clinico-demographic (i.e., tumour staging and the personal factors of age, comorbidities, baseline BMI, sex) and treatment-related function post-resection in patients with tongue and/or FOM cancer, with emphasis on speech and swallowing-related outcomes. The ultimate goal of this research is to determine if post-treatment prognostication related to function and QOL should be adapted based on various clinico-demographic and/or treatment-related factors. This information would be helpful in counselling patients prior to OCC treatment and may prompt different assessment and management algorithms for speech and swallowing in older individuals.

In addition to age, we will examine other personal factors and treatment-related variables believed to influence functional outcomes including comorbidities, sex, BMI, and tumour staging (t- and n-stage). In this way, the effects of patient-, disease- and treatment-related characteristics on speech and swallowing function can be controlled for in our exploration of age effects.

This study will address the following research questions:

1. What is the baseline speech and swallowing function of patients requiring treatment for tongue and/or FOM cancer? Are there clinico-demographic related predictors of baseline speech and swallowing function among these patients?
2. What is the immediate post-surgical speech and swallowing function of patients treated for tongue and/or FOM cancer? Does this function differ from baseline? Are there demographic and treatment-related predictors of speech and swallowing function immediately post-treatment among this patient population?
3. What is the long-term speech and swallowing function of patients treated for tongue and/or FOM cancer? Does this function differ from baseline and from immediately post-treatment? Are there demographic and treatment-related predictors of speech and swallowing function longer-term post-treatment among this patient population?

Chapter 2

2 Method

2.1 Participants

Retrospective review of electronic medical records yielded patient-, disease-, and treatment-related data of patients treated for oral cavity cancer at the LRCP between January 01, 2014, and December 31, 2017. This period was selected to align with the onset of coordinated functional outcomes data collection by the clinical speech-language pathologists (SLPs) at the LRCP. In addition, the length of the time frame was selected in an effort to achieve an appropriate sample size for this exploratory investigation. A sample size of 100 participants (or greater) is considered appropriate for research objectives that involve summarizing categorical and continuous data (Johnston, Lakzadeh, Donato & Szabo, 2019). On average, 400 individuals with head and neck cancer present to the LRCP each year. Of those, approximately 100 patients per year receive a diagnosis of oral cavity cancer (Mundi et al., 2018), and typically one third of those cases are cancers of the tongue and/or FOM. Given this historical information, we hypothesized that inclusion of new patients across four calendar years would provide a sample of approximately 100 patients.

The desired patient cohort included individuals over 18 years of age who were treated for a first-ever tongue or FOM cancer using surgery with a curative intent. Charts were excluded from this investigation if the patient 1) received primary non-surgical treatment (i.e., primary RT or CRT), 2) received non-curative treatment (i.e., palliative intent surgery, or comfort measures only), 3) was being treated for recurrent disease, 4) demonstrated evidence of recurrence within the first year following treatment, and/or 5) did not undergo functional outcomes measurement at baseline.

This study received ethical approval from the Western University Health Sciences Research Ethics Board (#119764).

2.2 Data Collection

Data was collected into an electronic database which was created on a cloud-based platform (REDCap), and housed on Lawson Health Research Institute's server. The database was created to capture the variables of interest, and the order of their appearance in the database reflected the sequential nature of patient visits to LRCP. As such, the database was utilized as a data collection form, with sequential pages (or tabs) appearing in a logical order that was parallel to the flow of information found within the medical records. Eligible patients were initially identified using the HN MDT clinic appointment lists which provided patient names and medical record numbers for all patients seen regarding a HNC diagnosis. Upon accessing eligible patients' electronic medical record, we located the 'Clinical Documents' tab in Powerchart (the electronic medical record platform used by LRCP) to identify the 'tumour board note' associated with the patient's initial visit to the HN MDT.

Information regarding patient-, disease-, and treatment-related data was often found in multiple chart locations, which provided opportunity to validate various data points. For example, the patient's date of birth typically appeared in both the header at the top of the medical chart, the 'patient information' tab, and in clinical notes dictated by members of the HN MDT. Table 1 outlines the most common document locations (e.g., tumour board notes, clinical notes, imaging reports, etc.) for each of the variables of interest. As a second strategy toward locating desired information, we also identified potential sources of information by scanning the list of document authors to locate dictations contributed by members of the HN MDT. Notes dictated by any surgical/radiation/medical oncologist, resident, or surgical fellow associated with the HN

MDT, as well as nurse practitioners and other health disciplines associated with HN patient care, were selected for review.

Table 1.

Data Collection from Electronic Patient Records

Chart Location	Variables of interest
Patient File Header	Age, sex, weight
Tumour Board Note	Disease site, TNM staging, primary and adjuvant treatment recommendations
Oncology Flowsheet	Weight, height
MDT Clinical Note	Age, sex, disease site, staging, recommendation treatment, comorbidities
Operative Note	Disease site, reconstruction, feeding tube status, tracheostomy tube status
Clinical Note (Surgical Clinic)	Disease site, reconstruction, feeding tube status, tracheostomy tube status, type of feeding tube
LRCP Note	Adjuvant treatment status, feeding tube status, type of feeding tube, discharge of feeding tube
SLP Clinical Note	FOIS level, PSS-HN scores, MDADI scores

2.2.1 Clinico-Demographic and Treatment Characteristics

Data collected from electronic medical records of consecutive eligible patients included: age at diagnosis, BMI, comorbidities, sex, oral cavity site of cancer, and tumour staging (t- and n-stage). This information was collated into the electronic database within REDCap.

Treatment-related data on surgical reconstruction, adjuvant treatment, and feeding tube use were gathered for use in post-treatment analyses. In addition, a comorbidity score (CCI score) was calculated using comorbidity information collected from the medical charts, in order to assign patients an index value that characterized their health comorbidities at the time of cancer diagnosis.

2.1.1.1 Charlson Comorbidity Index (CCI). To explore the effect of age and disease-related factors on functioning, the overall health state of an individual also needs to be understood. One method for capturing 'healthiness' retrospectively includes analysis of comorbid health conditions. The CCI, developed by Mary Charlson in 1987 (Charlson et al., 1987), is a weighted index that permits characterization of health comorbidities known to influence one's risk of death within one year of hospitalization, as well as 10-year mortality rates (Charlson et al., 1987). The modified version of the CCI (Deyo et al., 1992) takes account of 17 health conditions derived from the International Classification of Diseases (Deyo et al., 1992; World Health Organization, 1990).

The CCI categorizes comorbid conditions including diabetes mellitus, hypertension, chronic obstructive pulmonary disease, and dementia, among others (Deyo et al., 1992). This tool which assigns a comorbidity score that describes a patient's risk of death (0-1: low risk, 2-3: mild risk, 4-5: moderate risk, ≥6: severe risk; Charlson et al., 1987), has previously been used in studies of patients with oral cavity cancers (Ghanizada et al., 2021; Lee et al., 2016) to assess risk of death (Ghanizada et al., 2021). In scoring the CCI, each comorbidity category is assigned a weighting (e.g., one to six), which connotes an associated adjusted risk of death (Charlson et al., 1987). The weighted scores are summed across the 17 comorbidity categories, with a single comorbidity index derived for the patient. Since age is correlated with prognosis, Charlson and colleagues (1994) modified the scoring system of the CCI to include the patient's age (Charlson et al., 1994; Qu et al., 2020). The age-adjusted CCI incorporates age as a correction variable of the final score by adding one point for every decade over 40 years of age (Charlson et al., 1994; Qu et al., 2020). As such, a score of zero indicates that the patient has no comorbidities, while a higher score indicates both the presence of comorbidities and a higher risk of death (Charlson et al., 1987). In the present investigation, the modified age-adjusted CCI was used to derive a measure of comorbidity based on the presence of various comorbid conditions identified through medical chart review.

The reliability and validity of the CCI have been determined in various patient populations, including oncology (de Groot et al., 2003; Stavem et al., 2017). Previous retrospective chart and literature reviews have reported the scale's reliability (i.e., interrater reliability) and validity (de Groot et al., 2003; Hall et al., 2006; Stavem et al., 2017). Study authors have measured reliability using the intraclass correlation coefficient (ICC; a measure of how similar individuals are likely to assess the outcome) and have suggested that an ICC value of 0.75 represents excellent reliability (Hall et al., 2006; Stavem et al., 2017). With a reported ICC value of 0.76, these prior studies have demonstrated excellent interrater reliability, so that similar results can be expected when CCI ratings are completed by different raters (de Groot et al., 2003; Hall et al., 2006; Stavem et al., 2017). The scale's predictive validity also has been established using a variety of criterion measures (e.g., death, disability, length of hospital stay, etc.); significant relationships between the scale and these objective measures indicate that the items of the CCI are able to predict survival outcomes (de Groot et al., 2003; Hall et al., 2006).

2.2.2 Functional Characteristics

In HNC clinical care, outcomes are typically evaluated using a battery of assessment tools intended to document changes in speech and swallowing, as well as capture the impact of altered performance on one's function and QOL. Objective measurement of speech and swallowing that represent the level of body functions and structure in the ICF framework (WHO, 2001) typically requires the use of instrumental techniques to visualize physiological processes that are not directly observable through patient interactions. However, such techniques, including acoustic analysis of speech and videofluoroscopic and/or endoscopic evaluation of swallowing, are resource intensive, and are not used routinely in practice unless clinically indicated (Boaden et al., 2020; CASLPO, 2014; Fattori et al., 2016). Rather, clinician-rated measures of function and patient-reported outcome measures (PROMS) are often used as surrogate measures of physiological function to circumvent the more invasive, time consuming, and complex evaluations. Thus, data were collected from the medical charts of participants that reflected baseline and post-treatment speech and swallowing function representing the levels of activity and participation in the ICF framework, and swallowing-related QOL (see Figure 1).

As such, data were collected from S-LP documentation regarding the following measures that were administered in the context of clinical care: the PSS-HN, the FOIS, and the MDADI. In addition to collecting scores from baseline administration of these tools, data were also collected from assessment time points immediately following surgical treatment (i.e., prior to hospital discharge) and at 6-12 months post-treatment, as per routine speech and swallowing outcomes measurement by SLPs. These post-treatment time points were collected to explore associations between patient-, disease- and treatment-related factors and speech and swallowing function.

2.2.2.1 Performance Status Scale – Head and Neck (PSS-HN). The PSS-HN is a clinician-rated tool designed to capture functional performance with respect to eating and speaking through patient interviews (List et al., 1990). Three subscales permit description of performance in terms of three areas of functioning: diet (‘Normalcy of Diet’), speech (‘Understandability of Speech’), and social eating (‘Eating in Public’). Within each subscale, a hierarchically arranged list of items reflects a continuum from total incapacitation (score of zero) to full normal functioning (score of 100; List et al., 1990).

The PSS-HN ‘Normalcy of Diet’ (Diet) subscale reflects the degree to which an individual can eat a normal diet (List et al., 1990), with ten food categories arranged from easiest-to eat to hardest-to-eat. The PSS-HN (Diet) score reflects the highest ranking of foods currently consumed by the patient (i.e., the hardest-to-eat food), with a higher score indicating better swallow function (List et al., 1990). The PSS-HN ‘Understandability of Speech’ (Speech) subscale is a five-item scale that reflects the degree to which the individual's speech is understood, from “never understandable” to “always understandable”, with a higher score reflecting better speech function (List et al., 1990). Finally, the PSS-HN ‘Eating in Public’ (Eat) subscale reflects the degree to which the individual eats in public settings and in the presence of others (List et al., 1990). Because this scale relates to the interrelation of social factors and individual behaviour, this subscale is essentially measuring an individual’s psychosocial swallowing function. This subscale consists of five levels which range from "always eats alone" to "no restriction of place, food, or companion" (List et al., 1990). Each subscale of the PSS-HN is scored separately (List et al., 1990); as such, three subscale scores were gathered from patient charts in the current investigation.

The inter-rater reliability of the PSS-HN has been established using Kappa statistics, which describes the degree to which the rater's scores are in agreement with other raters; the higher the statistic, the more reliable the scale (List et al., 1990). All three subscales demonstrate high levels of interrater reliability, with Kappa statistics ranging between 0.64 and 0.88 (List et al., 1990). The authors of the PSS-HN have also examined the validity of the scale by evaluating its specificity and sensitivity to differences in levels of functioning in HNC patients (List et al., 1990). Validity of the PSS-HN was assessed using the Karnofsky Performance Scale (KPS) as it is a widely used measure of functional performance in cancer patients (List et al., 1990). Spearman correlations between the PSS-HN subscales and KPS demonstrated moderate correlation, ranging between 0.30 and 0.38, revealing that the PSS-HN subscales provide independent information that is not provided by KPS ratings (List et al.,1990). The authors determined that the scale is specific to HNC patients, is able to detect differences in groups of HNC patients expected to be functioning at different levels, and is more sensitive to the unique problems that HNC patients experience (List et al., 1990).

In the current investigation, the PSS-HN (Diet) and (Speech) subscale scores were collected as reported at baseline, and immediately and long-term post-operatively, from patient charts. The PSS-HN (Eat) subscale data were collected only at baseline and long-term post-operative time points because unlike the other subscales, the PSS-HN (Eat) is not administered immediately post-treatment as it does not represent a valid measure for patients who have been hospitalized for a period of time. That is, hospital in-patients do not have sufficient opportunities to eat in social settings.

2.2.2.2 M.D. Anderson Dysphagia Inventory (MDADI). The MDADI is a reliable and validated disease-specific questionnaire that assesses an individual's swallowing-related QOL (Chen et al., 2001). This tool is often used in clinical practice and research to assess changes in swallowing-related QOL following HNC treatment, with the understanding that dysphagia and associated QOL deficits are common consequences of treatment. Several seminal studies have employed the MDADI as a primary outcome measure in evaluating swallowing outcomes in HNC patients (Hutcheson et al., 2016; Lin et al., 2021; Nichols et al., 2019), indicating extensive adoption of the MDADI in the medical literature. Locally, the MDADI has been routinely included in the S-LPs' battery of clinical assessment tools, and data were available in the medical charts of most patients included in the current investigation.

The MDADI includes 20 items, with each item being rated on a 5-point Likert scale; the anchors of the five possible responses to each item include 'strongly agree', 'agree', 'no opinion', 'disagree', and 'strongly disagree' (Chen et al., 2001). This multidimensional inventory was developed to assess a variety of QOL domains as they relate to the experience of swallowing impairment including emotional, functional, and physical aspects. The emotional subscale, comprised of six items, consists of statements representing the individual's affective response to the swallowing disorder (Chen et al., 2001; Lin et al., 2021). The functional subscale, consisting of five items, captures the impact of the individual's swallowing problem on daily activities (Chen et al., 2001; Lin et al., 2021). Finally, the physical subscale, with eight items, represents self-perceptions of swallowing difficulty (Chen et al., 2001; Lin et al., 2021). In addition to these subscales, a global subscale (consisting of a single question) assesses the impact of an individual's swallowing difficultly on their daily activities (Chen et al., 2001).

Scores for each subscale are calculated by finding the mean score across items associated with each subscale (Chen et al., 2001; Cleeland et al., 2000). A composite score, which provides a summary of the MDADI as a weighted average, is calculated by averaging all item scores (except the 'global' item) and multiplying by 20, resulting in a composite score ranging from 20 (e.g., 1 point for every item) to 100 (e.g., 5 points for every item; Chen et al., 2011). Higher MDADI scores reflect better swallowing-related QOL (Chen et al., 2001). Additionally, the composite score can be used to document significant change in swallowing function. Hutcheson and colleagues have determined that a change of 10 points in the MDADI composite score is indicative of clinically meaningful differences in swallowing function (Hutcheson et al., 2016).

The reliability of the MDADI has been assessed using measures of internal consistency and test-retest reliability. Internal consistency was determined by using Cronbach's α coefficient (ranging between 0.85 and 0.93) and revealed that items of the MDADI address the desired content area (i.e., QOL related to swallowing; Chen et al., 2001). Test-retest reliability was evaluated by the authors of the tool with administration of the questionnaire at different time points (e.g., at the time of diagnosis and again 2 weeks later; Chen et al., 2001). The test-retest reliability coefficients of the subscales ranged from 0.69 to 0.88, revealing good to excellent reliability (Chen et al., 2001). Finally, criterion validity of the MDADI was determined using the Performance Status Scale (PSS-HN; Eat subscale) as the gold standard for measuring psychosocial aspects of swallowing (Chen et al., 2001). The MDADI and the PSS-HN (Eat) subscale demonstrate an acceptable level of correlation (correlations ranging between 0.47 and 0.61), establishing that the two scales both measure psychosocial aspects of swallowing (Chen et al., 2001).

All subscale and composite scores were gathered at baseline and long-term post-operatively from patient charts in the current investigation. Similar to the PSS-HN (Eat) subscale, the MDADI is not administered immediately post-treatment. This measure asks patients to rate items related to the impact of their swallowing impairment on their QOL based on their experiences in the past week; hospitalized in-patients are unlikely to have engaged in social or typical eating contexts in the reference time period.

2.2.2.3 Functional Oral Intake Scale (FOIS). The FOIS is a validated clinician-rated scale that provides a method for capturing an individual's mode of nutritional intake, that is by mouth (oral) or by feeding tube (enteral), as well as additional diet restrictions or compensations recommended to support safe and efficient oral intake (Crary et al., 2005). The FOIS is a seven-point ordinal scale that assigns a numeric score to one's functional level of oral intake of food and liquid, which ranges from complete dependence on tube feeding (1 point) to tolerance of an oral diet with no restrictions (7 points; Crary et al., 2005; Kotz et al., 2012). FOIS scores were collected from patients charts at baseline, and immediately and long-term post-operatively, in the current investigation. FOIS scores were also reported as a median, rather than a mean, as previously done in other studies (Crary et al., 2004; Yi & Shin, 2019). A median is preferred to mean because a median is less affected by outliers or extreme scores in the distribution, and when data is measured on an ordinal scale (Manikandan, 2011; Tenny & Hoffman, 2022).

While the FOIS was originally validated in patients experiencing dysphagia following a stroke, (Crary et al., 2005), this tool has been widely applied in other clinical populations at risk for swallowing impairment including neurodegenerative diseases, post-COVID-19 infection, and HNC (Hashida et al., 2021; Mofsky, 2012; Salvioni et al., 2021; Traugott et al., 2021; Yi & Shin, 2019). Crary and colleagues reported that the FOIS has adequate test-retest reliability, with correlations ranging between 0.98 and 0.99, even without specific training for raters (Crary et al., 2005). Criterion validity of the FOIS was established by using videofluoroscopic examination of swallowing function, revealing that the scale is significantly associated with the presence of dysphagia (significant correlations ranging between 0.26 and 0.54; Crary et al., 2005). The study ultimately revealed that FOIS ratings were significantly associated with dysphagia severity, but not with aspiration severity (Crary et al., 2005).

2.3 Statistical Analyses

Descriptive statistics were used to obtain measures of central tendency for all clinico-demographic and treatment-related variables, and all outcome variables. All statistical analyses within this investigation were performed using R statistical software (R Core Team, 2022). Bivariate associations for categorical outcomes (e.g., sex, reconstruction status, adjuvant therapy status) were analyzed using the chi-square test (Daniel & Cross, 2013). All outcome variables were then analyzed using the Shapiro-Wilk test to determine the normality of distribution and ultimately guide the choice of appropriate statistical tests (e.g., parametric vs. non-parametric). Comparable to the results of other studies using similar outcome measures (Hsiang et al., 2019; Ihara et al., 2022; Jovanovich et al., 2022), the MDADI subscales, the PSS-HN (Eat) subscale, and FT duration were normally distributed. Inspection of the FOIS data using a frequency histogram revealed a negative skew, indicating the distribution was non-normal; this was also confirmed using the Shapiro-Wilk test of normality. In contrast, the PSS-HN (Diet) and (Speech) subscales were positively skewed on visual inspection, and non-normality was confirmed using the Shapiro-Wilk test of normality. As such, parametric tests of difference (e.g., Linear Mixed Effects (LME), post-hoc paired t-test) were used to evaluate change over time with data from the MDADI subscales, and the PSS-HN (Eat). The remaining outcome measures were analyzed using non-parametric tests of difference (e.g., Friedman tests, post-hoc Wilcoxon signed rank test).

Before beginning the investigation, it was necessary to ensure that a sufficient sample size could be achieved for all analyses. Upon inspection of the dataset, it was evident that data were missing in both the 6- and 12-months post-operative visits, such that neither time point yielded sufficient case numbers. To address this, scores collected at the 6- and 12-month time points were analyzed using paired t-tests. The results of this analysis demonstrated that the scores gathered at the 6- and 12-months post-operative time points were not significantly different, and therefore these time points were collapsed, creating a single long-term time point. In cases where a single patient had data for each of these time points, the highest score was retained, in keeping with prior literature (Tuomi et al., 2020).

Within-group analyses were performed to determine if speech and swallowing function changed significantly across three time points - baseline, immediately post-surgery, and at long-term post-surgery. Immediately post-surgery, the FOIS and PSS-HN (Diet and Speech) scales are routinely collected in clinical practice; however, the other outcome measures (PSS-HN (Eat) and the MDADI subscales) are not typically administered, and data from these scales were, therefore, not available at this time point, as described previously. In our analyses, the functional outcome scores served as the dependent variables, and 'time' served as the independent variable.

Post-hoc analyses were performed when analyses of variance yielded statistically significant results to determine which pairwise comparisons accounted for the significant difference (Hogg & Tanis, 2016). Given that data were compared across three time points (1) Baseline vs. Immediately post-treatment; 2) Baseline vs. Long-term post-treatment; 3) Immediately post-treatment vs. Long-term post-treatment), the alpha level for the three post-hoc analyses was adjusted using a Bonferroni correction, to mitigate the increased risk of type I error (Armstrong, 2014). In this case, the Bonferroni correction translated into a *p* value of 0.017 to determine significance of post-hoc comparisons.

Some normally distributed variables (e.g., MDADI, PSS-HN (Eat) subscale) also presented with variability in sample size. Based on previous retrospective chart review investigations, variance was anticipated in the number of data points available across outcome measures. To address the potentially unequal samples, a Linear Mixed Effects (LME) analysis was used to test if a difference existed in speech and/or swallowing performance across time (Bates, Mächler, Bolker, & Walker, 2015; Harrison et al., 2018; Oberg, & Mahoney, 2007; Winter, 2013). Using an LME, it was possible to keep participants in the analysis whose data was missing at random (Bates, Mächler, Bolker, & Walker, 2015; Harrison et al., 2018; Oberg, & Mahoney, 2007). For the post-hoc analysis, dependent samples t-tests were used to compare all time points to one another (Mishra et al., 2019), with the alpha value of significance at 0.0083 using the Bonferroni correction. With varying sample sizes and variances at each time point, the Satterthwaite approximation was used to calculate the degrees of freedom for each t-test (DiSantostefano & Muller, 1995; Satterthwaite, 1946).

Relationships between clinico-demographic and treatment-related variables and the outcomes measures of interest were explored using correlation analyses (Guyatt et al., 1995). The point-biserial correlation coefficient (r_{pb}) was used to estimate the product-moment correlation in cases where one of the variables was dichotomous (i.e., reconstruction and adjuvant treatment status; Jacobs & Viechtbauer, 2017). Relationships between continuous variables (e.g., age and CCI) were evaluated using Pearson's coefficient (*r*; Brown & Hayden, 1985; Winters et al., 2010). The non-parametric equivalent test of correlation, the Spearman

Rank correlation coefficient (ρ), was used to evaluate the remaining relationships (Brown & Hayden, 1985; Winters et al., 2010).

Strength of correlation was described following the conventional approach of interpreting correlation coefficients based on the absolute magnitude (Mukaka, 2012; Schober, Boer, & Schewarte, 2018). In this approach, coefficients of 0.90-1.00 are interpreted as ‘very strong’ correlations, coefficients 0.70-0.89 are interpreted as ‘strong’ correlations, coefficients of 0.40-0.69 are interpreted as ‘moderate’ correlation, and coefficients of 0.10-0.39 and 0.00-0.09 are interpreted as ‘weak’ and ‘negligible’ correlations, respectively (Schober, Boer, & Schewarte, 2018). All statistical tests of correlations used an alpha value of 0.05 unless otherwise specified (Bujang & Baharum, 2016; Guenther, 1977; Serder et al., 2021).

Finally, multiple linear regression analyses were performed to determine if any clinico-demographic and treatment-related variables (or any combination of these variables) accounted for variance in speech and swallowing function as measured at baseline or at different post-treatment time points. Multiple linear regressions require assumptions (e.g., multicollinearity, homoscedasticity) to be made about the data that it represents, so that the models are appropriate approximations (Casson & Farmer, 2014). The first assumption is the independence of errors, where all outcomes are separate from each other (there are no duplicate responses). This was achieved through the creation of a REDCap database to ensure individual data was only entered into the dataset once. The second assumption is the absence of multicollinearity among the independent variables (e.g., since MDADI and PSS-HN (Eat) subscale scores are correlated, both should not be included in the same model). Multicollinearity in a regression model analysis occurs when two or more independent predictor variables are strongly or very-strongly correlated to each other (coefficients between 0.70 and 1.00; Gregorich et al., 2021), which results in the lack of unique information about the regression model (Casson & Farmer, 2014). This assumption was addressed after examining the relationships between the independent variables and omitting variables accordingly. Finally, homoscedasticity is the assumption of equal or similar variances in different groups being compared (Casson & Farmer, 2014). This assumption can be tested by the inspection of residual plots, where the "spread" of the points across the predicted values should be the same (Ernst & Albers, 2017). Inspection of the outcome measure data using residual plots revealed equal "spreads", indicating that this assumption was met. As all the assumptions of regression modelling were met, regression analyses were appropriate to conduct. In these analyses, independent variables (i.e., age at diagnosis, CCI, t-stage, n-stage, baseline BMI, reconstruction, adjuvant treatment, baseline outcome measures) were entered into separate regression models (i.e., one model per dependent variable) in a backwards stepwise approach to determine if any independent variables had a significant impact on the variance of the dependent variables (i.e., FOIS, PSS-HN, MDADI, FT duration; Weigand, 2010). The linear predictive models were expressed as an R^2 value, or the coefficient of multiple determination, as well as an estimate of the magnitude of their contribution, in order to represent the proportion of variance that was explained (Nakagawa et al., 2017). More specifically, the baseline variables of age at diagnosis, CCI, baseline BMI, sex, and tumor staging were included as potential predictors of speech and swallowing function at baseline. In evaluating speech and swallowing function immediately post-surgery, the variable of surgical reconstruction was also included in regression analyses. Finally, in examining long-term speech and swallowing function, the variables of adjuvant therapy status and FT duration were also included.

Chapter 3

3 Results

3.1 Clinico-Demographic and Treatment-Related Characteristics

Between 01 January 2014 and 31 December 2017, 1,349 patients presented to the Head and Neck multidisciplinary team at the LRCP for diagnostic assessment and treatment. Preliminary screening of the medical records of these 1,349 consecutive patients identified 72 patients with tongue and/or FOM cancers who were eligible for inclusion in this investigation.

In this sample population, 53 (73.6%) patients were male, and the average age at diagnosis was 61.5 years (standard deviation, ±10.6; range, 30-87 years). Information related to comorbid conditions was gathered and used to calculate the Charlson Comorbidity Index (CCI) for each patient. The majority of patients presented with a low (n=25) or mildly elevated (n=33) risk of death, based on the assigned CCI scores (Table 2). The average BMI among this patient cohort was 26.5 kg/m^2 (standard deviation, ± 6.7; range, 13.6 – 49.5 kg/m^2), suggesting that these patients are typically overweight. The most common oral cavity tumour subsite was the tongue (52 patients; 72.2%). The most common clinical tumour staging was T2 (34 patients; 47.2%), or tumours between 2 and 4 cm in their largest dimension, and the most common clinical nodal staging was N0 (37 patients; 51.4%), or no regional spread of disease.

Although all patients included in this investigation received primary surgical resection, some patients required additional surgical, oncologic, and medical interventions. For example, in cases of large surgical defects (typically associated with T2-T4 tumour staging), reconstruction using tissue transfer was deemed necessary to fill the resection defect. In this patient cohort, 57 patients (79.2%) underwent tissue reconstruction, with the majority of patients receiving a free flap tissue transfer (52 patients; 91.2%). In addition, some of the patients received adjuvant treatment (RT or CRT) based on their pathological risk for recurrence or distant metastasis as determined at the time of surgery. Thirty-nine patients (54.17%) received adjuvant treatment; radiotherapy (33 patients; 84.62%) was the most common adjuvant therapy regimen received. To support their nutritional health, 43 patients (59.7%) received a feeding tube, most of whom (n=30; 69.8%) underwent nasogastric tube insertion at the time of surgery. As a measure to protect the airway from acute surgical effects (e.g., edema), 61 patients (84.7%) also received a tracheostomy at the time of surgery.

Additional information on clinico-demographic and treatment-related characteristics are summarized before in Table 2.

Table 2.

Clinico-Demographics for Tongue and/or FOM Patients from 2014 to 2017

Characteristics	**Overall**
Number of participants	72
Age (years) at time of diagnosis	
Mean (SD)	61.5 (10.5)
Sex, N(%)	
Male	53 (73.6%)
Female	19 (26.4%)
BMI (kg/m^2)	
Mean (SD)	26.5 (6.7)
Age-adjusted Charlson Comorbidity Index (CCI) score	
Low risk (0-1)	25 (34.7%)
Mild risk (2-3)	33 (45.8%)
Moderate risk (4-5)	11 (15.3%)
Severe risk (>6)	3 (4.2%)
Charlson 10-year probability (%)	
Mean (SD)	79.0 (26.3)
Site of Cancer, N(%)	
Tongue	52 (72.2%)
Floor of Mouth	20 (27.8%)
Clinical T-stage, N(%)	
T1	9 (12.5%)
T2	34 (47.2%)
T3	15 (20.8%)
T4	14 (19.4%)
Clinical N-Stage, N(%)	
NX	7 (9.7%)
N0	37 (51.4%)
N1	9 (12.5%)
N2	19 (26.4%)
Type of feeding tube used, N(%)	
Gastrostomy	10 (13.8%)

Gastrostomy-Jejunostomy	2 (2.8%)
Nasogastric	30 (41.7%)
Unknown	1 (1.4%)
No feeding tube used	29 (40.3%)
Days feeding tube used	
Mean (SD)	71.2 (161.78)
Adjuvant therapy regimen, N(%)	
Radiotherapy	16 (22.2%)
Chemo-radiotherapy	23 (31.9%)
No adjuvant therapy	33 (45.8%)
Reconstruction type, N(%)	
Locoregional flap	1 (1.4%)
Pedicled flap	1 (1.4%)
Free flap	52 (72.2%)
Unknown	3 (4.2%)
No reconstruction	15 (20.8%)
Tracheostomy received, N(%)	61 (84.7%)

SD = standard deviation

3.2 Functional Measures of Speech and Swallowing

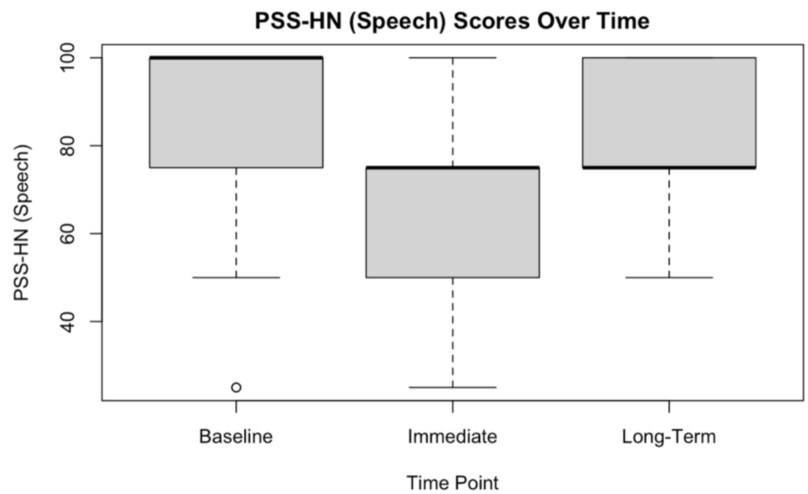
Functional outcomes data were gathered from medical chart documentation of speech and swallowing evaluations completed at baseline (i.e., prior to surgery), early post-surgery, and 6-to-12 months post-surgery, and were entered into a study-specific electronic database (REDCap).

3.2.1 Speech Function

The central tendency (mean [±SD]) for the PSS-HN (Speech) subscale scores were determined at baseline (91.0 [±23.3]), immediately post-treatment (68.2 [±23.3]), and long-term (80.2 [±14.8]) post treatment (Table 3; Figure 2). Repeated measures analysis of the PSS-HN (Speech) subscale revealed that speech function was significantly different across time (p <.001). Follow-up post-hoc analyses demonstrated that baseline PSS-HN (Speech) scores were significantly higher than scores immediately post-treatment (p <.001) and long-term post-treatment (p =.006), even though significant gains were demonstrated between immediate post-treatment and long-term follow-up (p = .006; Table 4).

Figure 2

PSS-HN (Speech) Scores Over Time



Note. Distribution of PSS-HN (Speech) scores across different pre- and post-treatment time points.

Table 3.

Repeated Measures Analysis Summary

Outcome Measures	Mean [SD] Baseline	Immediately Post-Tx	Long-Term Post-Tx	*p*-value
FOIS[a]	6.0 (7.0 – 5.0) (n=72)	5.0 (5.0 – 3.5) (n=51)	5.0 (5.0 – 5.0) (n=39)	<.001**
PSS (Diet)	63.5 [25.4] (n=72)	32.5 [14.9] (n=49)	52.3 [21.8] (n=39)	<.001**
PSS (Speech)	91.0 [16.9] (n=72)	68.2 [23.3] (n=37)	80.2 [14.8] (n=34)	<.001**
PSS (Eat)	66.7 [33.8] (n=72)	N/A[b] (n=6)	49.2 [28.7] (n=32)	.012*
MDADIg	71.9 [30.0] (n=72)	N/A [b] (n=2)	80.0 [25.3] (n=16)	.051
MDADIf	79.0 [18.5] (n=72)	N/A [b] (n=2)	81.3 [14.4] (n=16)	.228
MDADIe	77.9 [19.2] (n=72)	N/A [b] (n=2)	75.5 [19.4] (n=16)	.311
MDADIp	72.5 [20.3] (n=72)	N/A [b] (n=2)	73.2 [16.4] (n=16)	.076
MDADIc	81.9 [17.2] (n=72)	N/A [b] (n=2)	77.3 [15.5] (n=16)	.162

$p \leq 0.05$ is denoted as *; $p \leq 0.001$ is denoted as **

[a]FOIS scores are presented as median (interquartile range; IQR).

[b]PSS (Eat) and MDADI data are not available immediately post-treatment as they are not routinely administered while patients are in hospital.

Table 4.

Post-Hoc Analysis Summary for Significant Repeated Measures Analyses

Variable	Time Points Compared	p value
FOIS	Baseline v. Immediately Post-Treatment	<.001*
	Baseline v. Long-Term	.007*
	Immediately Post-Treatment v. Long-Term	.010*
PSS-HN (Diet)	Baseline v. Immediately Post-Treatment	<.001*
	Baseline v. Long-Term	.048
	Immediately Post-Treatment v. Long-Term	.002*
PSS-HN (Speech)	Baseline v. Immediately Post-Treatment	<.001*
	Baseline v. Long-Term	.006*
	Immediately Post-Treatment v. Long-Term	.006*
PSS-HN (Eat)	Baseline v. Long-Term Post-Treatment	.008*

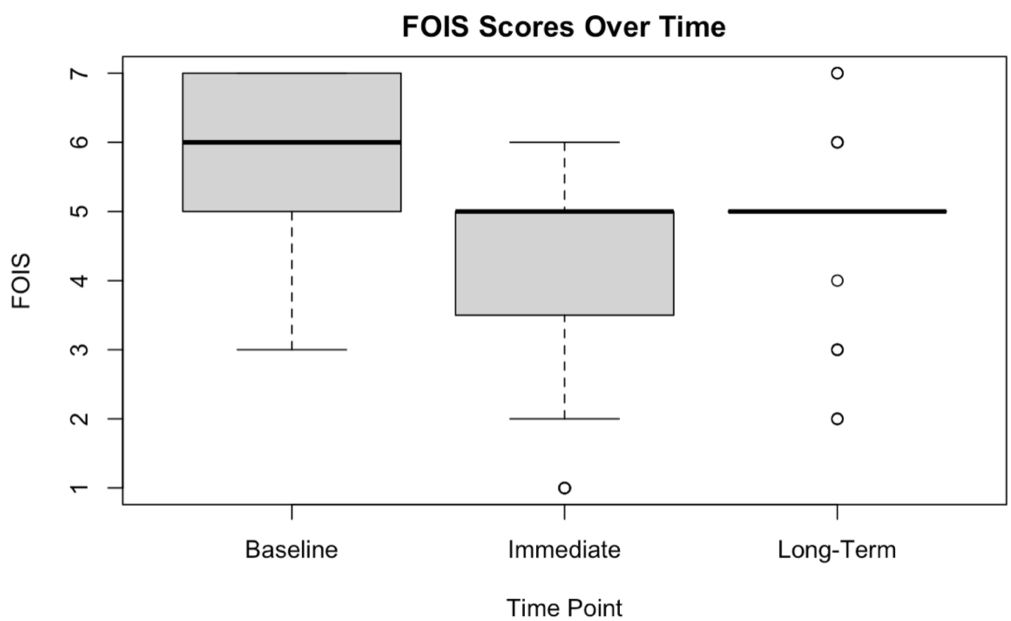
$p = .017$* (Bonferroni Correction)

3.2.2 Swallowing Function

The central tendency (median [IQR]) was determined for FOIS scores as measured at baseline (6.0 [5.0-7.0]), immediately post-treatment (5.0 [3.5-5.0]), and long-term (5.0 [5.0-5.0]) post treatment (Table 3; Figure 3). Repeated measures analysis demonstrated that swallow function as measured using the FOIS was significantly different across time ($p < .001$). Follow-up post-hoc analyses revealed that baseline FOIS scores were significantly higher than FOIS scores immediately post-treatment ($p < .001$) and long-term ($p = .007$) post-treatment. FOIS scores immediately post-treatment were also significantly lower than long-term post-treatment ($p = .010$; Table 4).

Figure 3

FOIS Scores Over Time

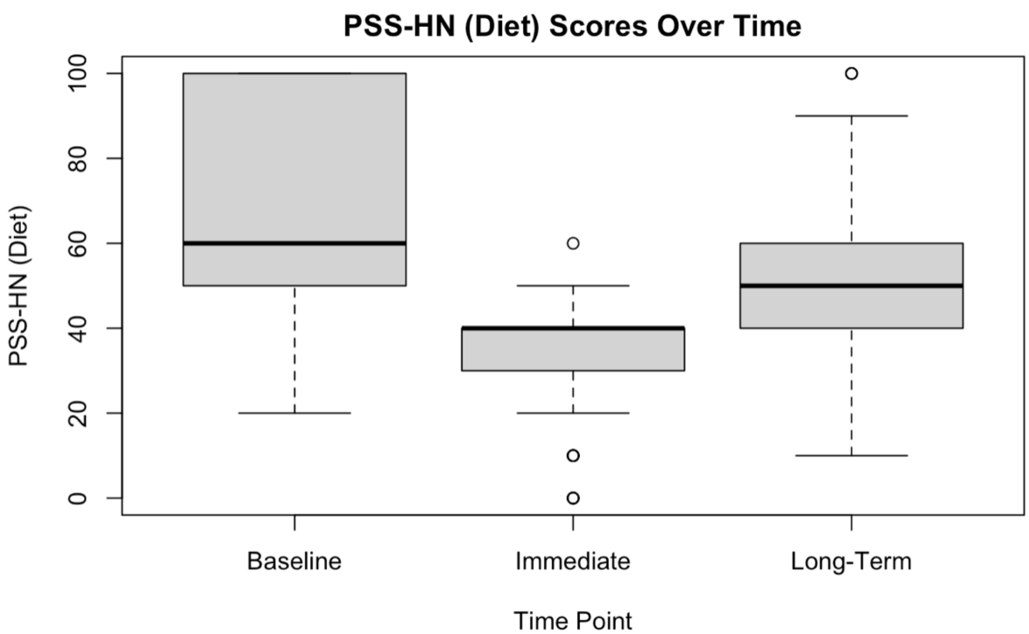


Note. Distribution of FOIS scores across different pre- and post-treatment time points.

Descriptive statistics were used to determine central tendency (mean [±SD]) for the PSS-HN (Diet) subscale scores at baseline (63.5 [±25.4]), immediately post-treatment (32.5 [±14.9]), and long-term (52.3 [±21.8]) post treatment (Table 3; Figure 4). Similar repeated measures analysis demonstrated that swallow function as measured using the PSS-HN (Diet) subscale was significantly different across time ($p < .001$). Follow-up post-hoc analyses revealed that PSS-HN (Diet) scores significantly declined immediately post-treatment compared to baseline ($p < .001$), and scores significantly improved at long-term follow-up compared to immediate post-treatment values ($p = 0.002$) and were no longer significantly different from baseline (Table 4).

Figure 4

PSS-HN (Diet) Scores Over Time

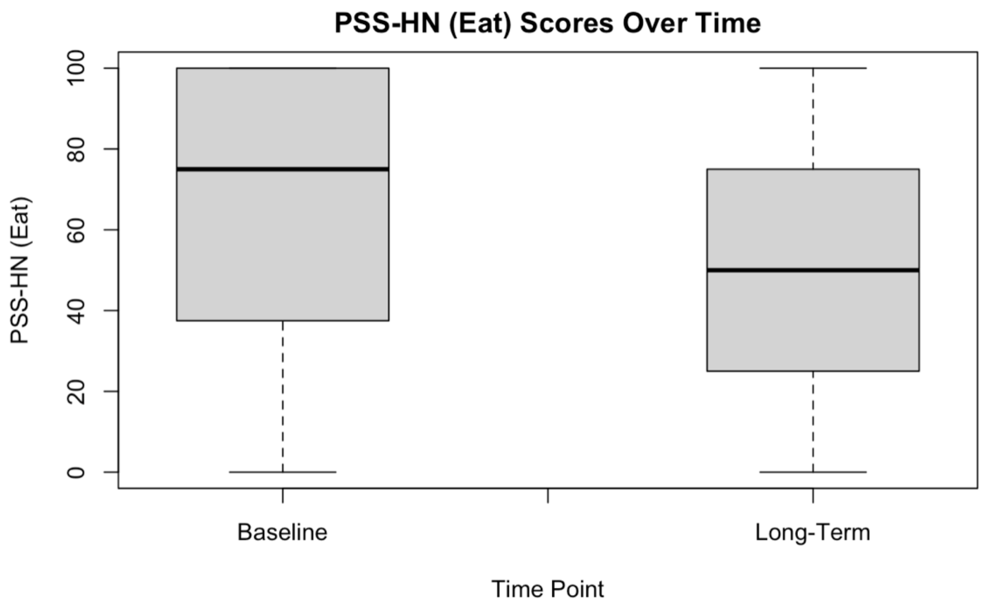


Note. Distribution of PSS-HN (Diet) scores across different pre- and post-treatment time points.

The central tendency (mean [±SD]) for the PSS-HN (Eat) subscale scores were determined at baseline (66.7 [±33.8]) and long-term (49.2 [±28.7]) post treatment (Table 3; Figure 5). Repeated measures analysis of the PSS-HN (Eat) subscale revealed that psychosocial swallowing was significantly different across time ($p = .012$). Follow-up post-hoc analyses revealed a significant decline in PSS-HN (Eat) scores over time (p = .008), without return to baseline function at long term follow-up (Table 4).

Figure 5

PSS-HN (Eat) Scores Over Time



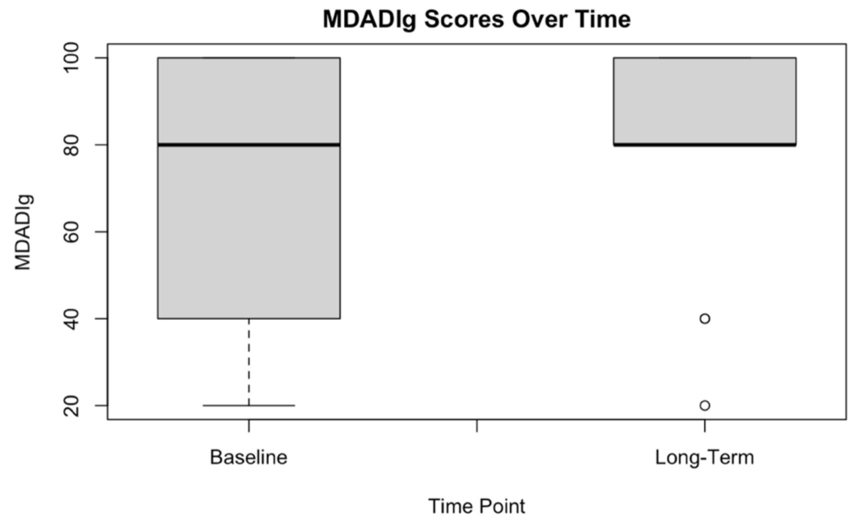
Note. Distribution of PSS-HN (Eat) scores across different pre- and post-treatment time points.

3.2.3. Swallowing-Related QOL

Measures of central tendency (mean [±SD]) were calculated using descriptive statistics for all of the MDADI subscales at baseline (MDADIg: 71.9 [±30.0]; MDADIf: 79.0 [±18.5]; MDADIe: 77.9 [±19.2]; MDADIp: 72.5 [±20.3]; MDADIc: 81.9 [±17.2]) and long-term post-treatment (MDADIg: 80.0 [±25.3]; MDADIf: 81.3 [±14.4]; MDADIe: 75.5 [±19.4]; MDADIp: 73.2 [±16.4]; MDADIc: 77.3 [±15.5]; Table 3; Figures 6, 7, 8, 9, and 10). None of the MDADI subscales demonstrated significant differences when comparing scores across time.

Figure 6

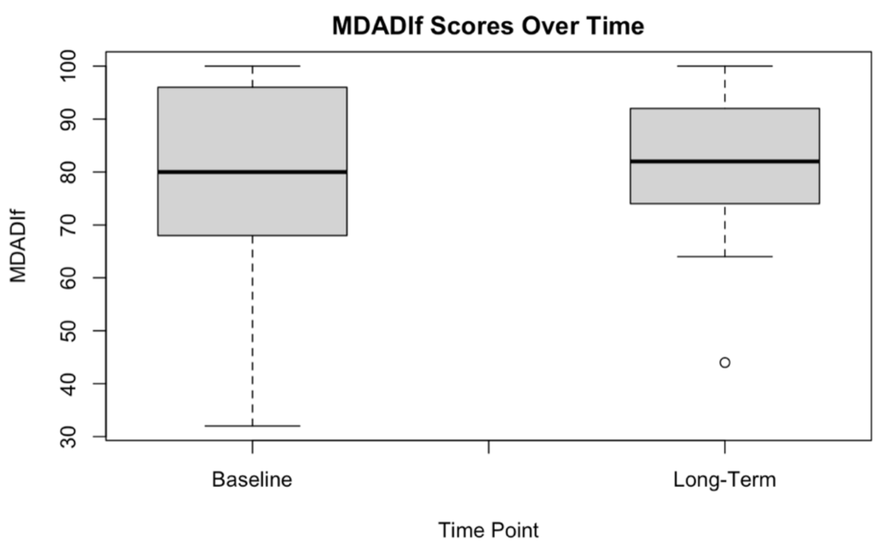
MDADIg Scores Over Time



Note. Distribution of MDADIg scores across different pre- and post-treatment time points.

Figure 7

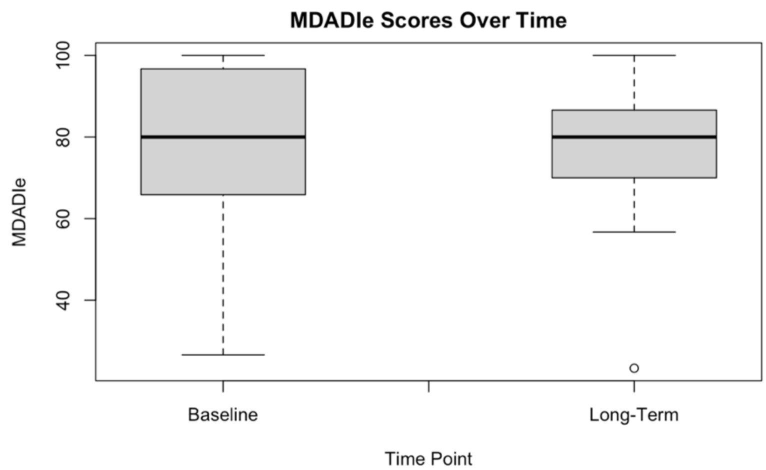
MDADIf Scores Over Time



Note. Distribution of MDADIf scores across different pre- and post-treatment time points.

Figure 8

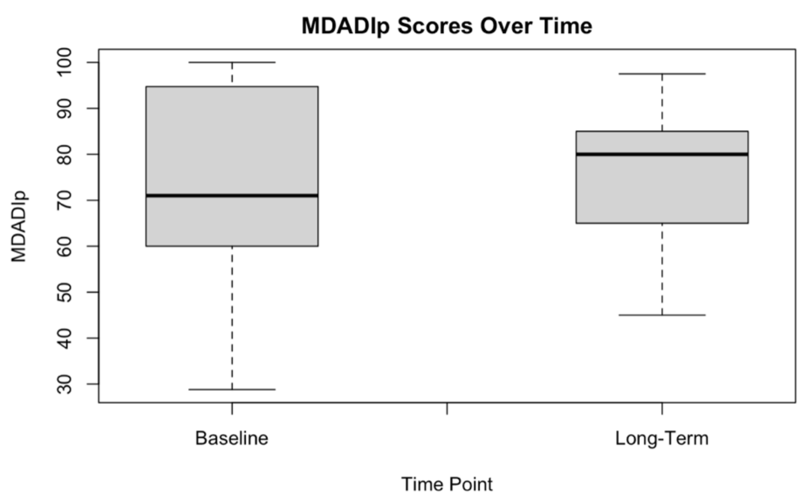
MDADIe Scores Over Time



Note. Distribution of MDADIe scores across different pre- and post-treatment time points.

Figure 9

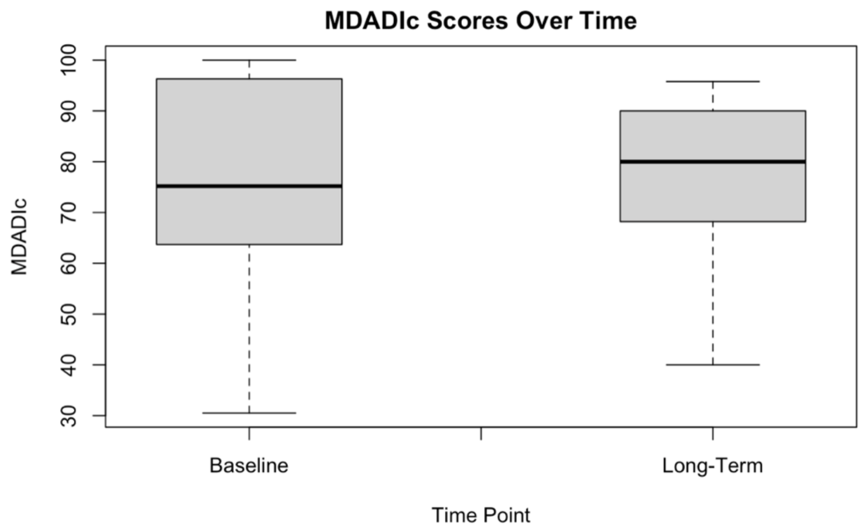
MDADIp Scores Over Time



Note. Distribution of MDADIp scores across different pre- and post-treatment time points.

Figure 10

MDADIc Scores Over Time



Note. Distribution of MDADIc scores across different pre- and post-treatment time points.

3.2 Correlation

3.2.1 Correlation at Baseline

Correlation analyses were conducted using baseline data to evaluate associations between the independent variables of interest (e.g., age at diagnosis, sex, CCI, t-stage, n-stage, baseline BMI), and speech and swallowing function before treatment (e.g., FOIS, PSS-HN, MDADI). Correlation coefficients were calculated among the twelve clinico-demographic related variables and pre-treatment speech and swallowing outcomes. Correlation coefficients relevant to the relationships between the clinico-demographic characteristics and outcomes are described herein; all coefficients and their respective level of significance are reported in Table 5.

The correlational analyses revealed 65 out of 91 correlations were statistically significant at baseline. Although most relationships between the patient-related characteristics were non-significant, there was a very strong positive correlation between age and CCI ($\rho = 0.85$, $p \leq 0.05$), and a moderate positive correlation between (clinical) t-stage and (clinical) n-stage ($\rho = 0.50$, $p \leq 0.05$). All baseline measures of speech and swallowing demonstrated significant moderate correlations with t-stage at baseline. Additionally, all baseline MDADI subscale scores demonstrated significant weak correlations with CCI scores at baseline. Age at diagnosis was weakly correlated with MDADIg scores at baseline ($\rho = 0.23$, $p \leq 0.05$). Finally, all measures of speech and swallowing function were moderately-to-very strongly associated with each other at baseline. A complete summary of the correlation results appears in Table 5.

Table 5.

Correlations at Baseline

	Sex	CCI	T-stage	N-Stage	BMI	FOIS	PSS (Diet)	PSS (Speech)	PSS (Eat)	MDADIg	MDADIf	MDADIe	MDADIp	MDADIc
Age	-0.14	0.85*	-0.27	-0.22	0.11	0.06	0.08	0.22	0.10	0.23*	0.16	0.21	0.21	0.17
Sex	1.00	0.04	0.16	0.02	0.09	-0.06	-0.08	-0.09	-0.10	-0.25	-0.11	-0.15	-0.17	-0.16
CCI		1.00	-0.27	-0.21	0.27	0.06	0.09	0.19	0.13	0.28*	0.28*	0.30*	0.30*	0.30*
T-stage			1.00	0.50*	-0.05	-0.38**	-0.43**	-0.46**	-0.42**	-0.43**	-0.49**	-0.48**	-0.48**	-0.52**
N-Stage				1.00	-0.30	-0.34**	-0.28*	-0.18	-0.28*	-0.19	-0.30**	-0.26*	-0.26*	-0.32**

BMI					1.00	0.27*	0.37**	0.17	0.26*	0.15	0.23	0.26	0.26*	0.25*
FOIS						1.00	0.79**	0.40**	0.66**	0.54**	0.53**	0.52**	0.52**	0.59**
PSS (Diet)							1.00	0.50**	0.77**	0.60**	0.62**	0.70**	0.70**	0.68**
PSS (Speech)								1.00	0.60**	0.55**	0.52**	0.46**	0.46**	0.58**
PSS (Eat)									1.00	0.60**	0.50**	0.55**	0.54**	0.58**
MDADIg										1.00	0.69**	0.67**	0.64**	0.71**
MDADIf											1.00	0.89**	0.72**	0.91**
MDADIe												1.00	0.80**	0.95**

MDADIp													1.00	0.93**
MDADIc														1.00

p≤0.05 is denoted as *; *p*≤0.01 is denoted as **

3.2.2 Correlations Immediately Post-Treatment

Correlation analyses also were conducted to evaluate associations between the clinico-demographic independent variables of interest (e.g., age at diagnosis, sex, CCI, t-stage, n-stage, baseline BMI), and speech and swallowing outcomes immediately post-treatment (e.g., FOIS, PSS-HN (Diet and Speech) scales). In addition to these baseline clinico-demographic variables, surgical reconstruction status was added as variable of interest.

As described in Chapter 2, PSS-HN (Eat) and MDADI data were not collected immediately post-treatment. Thus, correlation coefficients were calculated among the nine clinico-demographic related variables and the speech and swallowing outcomes collected immediately post-surgery. Correlation coefficients relevant to the relationships between the clinico-demographic and treatment-related characteristics and outcomes are described herein. All other correlation coefficients and their respective level of significance are reported in Table 6, although tabular data of previously reported correlations amongst clinico-demographic variables have been omitted.

Immediately post-treatment, reconstruction status demonstrated significant moderate negative associations with age at diagnosis (r_{pb} = -0.43, $p \leq 0.001$) and CCI scores (r_{pb} = -0.41, $p \leq 0.001$), and a significant moderate positive association with t-stage (r_{pb} = 0.43, $p \leq 0.001$). The FOIS and PSS-HN (Diet and Speech) subscale scores remained moderately-to-very strongly associated with each other immediately post-treatment.

Table 6.

Correlations at Immediate Post-Treatment

	Recon Status	FOIS	PSS (Diet)	PSS (Speech)
Age	-0.43**	-0.12	0.19	0.06
Sex	0.16	-0.01	0.06	0.18
CCI	-0.41**	-0.06	0.25	-0.04
T-stage	0.43**	-0.29*	-0.35*	-0.30
N-Stage	0.31**	-0.25	-0.13	-0.29
BMI	-0.04	0.00	0.02	0.06

Recon Status	1.00	-0.24	-0.28	-0.29
FOIS		1.00	0.71**	0.67**
PSS (Diet)			1.00	0.73**
PSS (Speech)				1.00

p≤0.05 is denoted as *; *p*≤0.01 is denoted as **

3.2.3 Correlation Long-Term Post-Treatment

Correlation analyses were conducted to evaluate associations between the independent variables of interest and speech and swallowing outcomes long-term post-treatment (e.g., FOIS, PSS-HN, MDADI). In addition to the previously described baseline clinico-demographic and treatment variables, adjuvant treatment status was added as an independent variable, and feeding tube duration was added as an outcome measure.

Correlation coefficients relevant to the relationships between the clinico-demographic and treatment-related characteristics and outcomes are described herein. All other correlation coefficients and their respective level of significance are reported in Table 7, although previously reported correlations amongst clinico-demographic variables have been omitted from Table 7.

In this analysis, adjuvant treatment status demonstrated a significant moderate negative association with PSS-HN (Diet) and PSS-HN (Eat) subscale scores at the long-term post-treatment time point (r_{pb} = -0.53, $p \leq .001$; r_{pb} = -0.59, $p \leq .001$, respectively).

Table 7.

Correlations at Long-Term Post-Treatment

	Adj Tx	FOIS	PSS (Diet)	PSS (Speech)	PSS (Eat)	MDADIg	MDADIf	MDADIe	MDADIp	MDADIc	FT duration
Age	-0.09	-0.23	-0.07	0.12	-0.10	0.18	-0.15	0.21	0.22	-0.14	-0.20
Sex	0.33**	-0.12	-0.22	-0.13	-0.08	0.21	0.03	0.05	-0.07	-0.02	-0.05
CCI	0.04	-0.21	-0.10	0.05	-0.25	0.04	-0.15	0.25*	0.30*	-0.24	-0.17
T-stage	0.08	-0.14	-0.24	-0.31	-0.21	-0.30	-0.16	-0.50**	-0.48**	0.11	0.30
N-Stage	0.04	-0.28	-0.34*	-0.23	-0.22	0.11	0.17	-0.26*	-0.26*	0.31	0.39
BMI	-0.04	0.03	0.18	-0.15	0.22	-0.34	-0.14	0.19	0.26*	-0.02	-0.34

Recon Status	0.15	-0.17	-0.28	-0.25	-0.10	0.13	-0.05	0.12	0.27	0.18	0.13
Adj Tx	1.00	-0.27	-0.53**	-0.24	-0.59**	0.00	-0.07	-0.38	-0.07	-0.17	0.25
FOIS		1.00	0.72**	0.44*	0.37*	-0.38	-0.46	0.19**	0.13**	-0.33	0.16
PSS (Diet)			1.00	0.38*	0.62**	0.09	0.16	0.37**	0.37**	0.20	0.14
PSS (Speech)				1.00	0.31	0.39	0.18	0.24**	0.11**	0.25	-0.46*
PSS (Eat)					1.00	0.28	0.27	0.37**	0.21**	0.43	-0.48*
MDADIg						1.00	0.84**	0.29**	0.13**	0.79**	0.26
MDADIf							1.00	0.89**	0.72**	0.90**	0.47

MDADIe								1.00	0.80**	0.95**	-0.09
MDADIp									1.00	0.93**	-0.08
MDADIc										1.00	0.31
FT duration											1.00

p≤0.05 is denoted as *; *p*≤0.01 is denoted as **

3.3 Regression

Multiple linear regression analyses examined whether variance in speech and swallowing function could be predicted by clinico-demographic and/or treatment-related variables at various assessment time points. Given that appropriate independent variables differed at each time point, separate regression analyses were completed at each time point for each outcome measure. However, since the subscales of the MDADI demonstrated strong to very strong correlations among themselves, only the MDADI composite subscale was entered into regression analyses as a dependent variable while all subscales were retained as independent variables. Additionally, because age at diagnosis and CCI were strongly correlated, age was excluded as an independent variable as it was also captured in CCI, thus meeting the multicollinearity assumptions of regression analyses.

3.3.1 Regression Analysis at Baseline

Multiple regression analyses were conducted to predict speech and swallowing function at baseline as measured using the FOIS, PSS-HN, and MDADIc, with the clinico-demographic variables (i.e., sex, CCI, t-stage, n-stage, BMI) of interest entered as potential predictors. A backwards stepwise approach was employed to determine which independent variables had a significant impact on the variance of the dependent variables (i.e., FOIS, PSS-HN, MDADIc).

For the PSS-HN (Speech) subscale, t-stage was the only independent variable that accounted for a significant, yet small amount of variance (R^2 = 0.19, adjusted R^2 = 0.18, F (1,70) = 16.84, $p \leq 0.01$). This demonstrates that approximately 18.0% of the variance of PSS-HN (Speech) scores can be accounted for by t-stage.

With respect to the FOIS, regression analysis demonstrated that t-stage and BMI accounted for a significant, yet small amount of the variance in these scores (R^2 = 0.20, adjusted

$R^2 = 0.18$, $F (2,69) = 8.81$, $p \leq 0.01$). This indicates that approximately 18.0% of the variance of FOIS scores can be accounted for by the linear combination of t-stage and BMI.

These same predictors accounted for a significant, yet small proportion of the variance in PSS-HN (Diet) scores at baseline ($R^2 = 0.29$, adjusted $R^2 = 0.26$, $F (2,69) = 13.73$, $p \leq 0.01$), as well as PSS-HN (Eat) scores at baseline ($R^2 = 0.28$, adjusted $R^2 = 0.26$, $F (2,69) = 13.64$, $p \leq 0.01$). This reveals that approximately 26.0% of the variance of PSS-HN (Diet) and 26.0% of the variance of PSS-HN (Eat) scores can be accounted for by the linear combination of t-stage and BMI.

With respect to the MDADIc, the results of this analysis indicated that t-stage alone accounted for a significant, yet small proportion of variance in MDADIc scores ($R^2 = 0.25$, adjusted $R^2 = 0.24$, $F (1,70) = 23.74$, $p \leq 0.01$). This demonstrates that approximately 18% of the variance of MDADIc scores can be accounted for by t-stage. Results of these regression analyses using baseline functional data are summarized in Table 8.

Table 8.

Multiple Linear Regression: Baseline Time Point

Predictor	**Outcome Measure** *FOIS*	*PSS-HN (Diet)*	*PSS-HN (Speech)*	*PSS-HN (Eat)*	*MDADIc*
Sex					
CCI					
T-stage	-0.29**	-8.25**	-6.37**	-13.39**	-7.76**
N-Stage					
BMI	0.04*	1.25**		1.07*	
Adjusted R^2	0.18**	0.26**	0.18**	0.26**	0.24**

p≤0.05 is denoted as *; *p*≤0.01 is denoted as **

3.3.2 Regression Analysis Immediately Post-Treatment

Multiple regression analyses were conducted to predict speech and swallowing outcomes, as measured using the FOIS and PSS-HN (Diet and Speech) subscales, with the clinico-demographic and treatment-related variables of interest entered as potential predictors. A backwards stepwise approach was employed to determine which independent variables had a significant impact on the variance of the dependent variables (i.e., FOIS, PSS-HN (Diet and Speech) subscales).

With respect to the FOIS, regression analysis demonstrated that only t-stage accounted for a significant, yet small amount of the variance in these scores ($R^2 = 0.13$, adjusted $R^2 = 0.11$, F (1,49) = 7.23, $p \leq 0.01$). This indicates that approximately 11.0% of the variance of FOIS scores can be accounted for by t-stage at this time point.

For the PSS-HN (Diet) subscale, only t-stage accounted for a significant, yet small proportion of the variance in PSS-HN (Diet) scores immediately post-treatment ($R^2 = 0.18$, adjusted $R^2 = 0.16$, F (1,47) = 10.26, $p \leq 0.01$). This reveals that approximately 16.0% of the variance of PSS-HN (Diet) scores can be accounted for t-stage.

Finally, with respect to the PSS-HN (Speech) subscale, CCI scores, t-stage, and reconstruction status accounted for a significant, yet moderate amount of variance in PSS-HN (Speech) scores ($R^2 = 0.30$, adjusted $R^2 = 0.24$, F (3,33) = 4.70, $p \leq 0.01$) in scores at this time point. This demonstrates that approximately 42.0% of the variance of PSS-HN (Speech) scores can be accounted for by the linear combination of CCI scores, t-stage, and reconstruction status at this time point.

Table 9.

Multiple Linear Regression: Immediately Post-Treatment Time Point

	Outcome Measure		
Predictor	*FOIS*	*PSS-HN (Diet)*	*PSS-HN (Speech)*
CCI			
Sex			-4.31
T-stage	-0.48**	-5.88**	-8.28*
N-Stage			
BMI			
Reconstruction (+/-)		-9.81	-27.80*
Adjusted R^2	0.11**	0.16	0.24**

p≤0.05 is denoted as *; *p*≤0.01 is denoted as **

3.3.3 Regression Analysis Long-Term Post-Treatment

Multiple regression analyses were conducted to identify predictors of long-term post-treatment speech and swallowing outcomes as measured using the FOIS, PSS-HN, MDADIc, and FT duration. A backwards stepwise approach was employed to determine which clinico-demographic and treatment-related variables had a significant impact on the variance of the dependent variables (i.e., FOIS, PSS-HN, MDADIc, FT duration).

With respect to the FOIS, no linear combination of independent variables reached significance at this time point.

With respect to the PSS-HN (Diet) subscale, the independent variables of CCI scores, t-stage, reconstruction status and adjuvant therapy status accounted for a significant, yet small amount of the variance in PSS-HN (Diet) scores long-term post-treatment ($R^2 = 0.45$, adjusted $R^2 = 0.38$, $F(4,34) = 6.93$, $p \leq 0.01$). This reveals that approximately 38.0% of the variance of PSS-HN (Diet) scores can be accounted for by the linear combination of CCI scores, t-stage, reconstruction status and adjuvant therapy status at this time point.

For the PSS-HN (Speech) subscale, no linear combination of independent variables reached significance at this time point.

With respect to the PSS-HN (Eat) subscale, the combination of CCI scores, t-stage, and adjuvant therapy status accounted for a significant proportion of variance in PSS-HN (Eat) scores ($R^2 = 0.51$, adjusted $R^2 = 0.46$, $F(3,28) = 9.64$, $p \leq 0.01$). This reveals that approximately 46.0% of the variance of PSS-HN (Eat) scores can be accounted for by the stated linear combination at this time point.

In the regression analysis for the MDADIc, no linear combination of independent variables reached significance at this time point.

Finally, regression analyses with FT duration demonstrated that sex, n-stage, reconstruction status and adjuvant therapy status accounted for a significant, yet small proportion of variance in FT duration (R^2 = 0.27, adjusted R^2 = 0.22, F 4,67) = 6.13, $p \leq 0.01$). This reveals that approximately 22.0% of the variance of FT duration can be accounted for by the linear combination of sex, n-stage, reconstruction and adjuvant therapy at this time point.

Results of these regression analyses using long-term post-treatment functional outcomes data are presented in Table 10.

Table 10.

Multiple Linear Regression: Long-Term Post-Treatment Time Point

Predictor	**Outcome Measure**					
	FOIS	*PSS-HN (Diet)*	*PSS-HN (Speech)*	*PSS-HN (Eat)*	*MDADIc*	*FT Duration*
Sex						0.19
CCI	-0.18	-4.63*		-6.30**	-2.53	
T-stage	-0.32	-4.99	-3.85	-7.57		
N-Stage						0.05
BMI			-0.67			
Reconstruction (+/-)		-18.44				0.38**
Adjuvant Therapy (+/-)	-0.67	-21.25**	-8.39	-32.10**		0.16
Adjusted R^2	0.09	0.38**	0.12	0.46**	0.06	0.22**

$p \leq 0.05$ is denoted as *; $p \leq 0.01$ is denoted as **

Chapter 4

4 Discussion

Patients diagnosed and treated for tongue and/or FOM cancers often already have difficulty with speech and swallowing at baseline, which may lead to worsened difficulties after resection (Haughey, 1993; Son et al., 2015). This study investigated the natural history of speech and swallowing function of patients treated for OCCs of the tongue and/or FOM, and examined relationships among clinico-demographic and treatment-related variables and speech and swallowing performance. The primary focus was to evaluate and compare specific outcome variables at three treatment time points: at baseline (pre-treatment), and immediately post-treatment, and long-term (6- to 12-months) post-treatment. Analyses were completed to i) document change in speech and swallowing function over time and ii) determine if relationships exist between the speech and swallowing outcomes and patient-, disease-, and treatment-related variables. A secondary objective of this study sought to focus on the contribution of age to speech and swallowing outcomes. In general, changes in speech and swallowing function are expected immediately after surgery, and while these functions improve in the long-term, function often does not return to baseline function. The trajectory of speech and swallowing function postoperatively in OCCs may be explained by the interplay of clinico-demographic and treatment-related characteristics. More specifically, the combination of comorbidity, tumour staging, and adjuvant treatment status, is likely able to predict a patient's swallowing ability post-treatment. The search for other meaningful predictors of speech and swallowing and QOL outcomes may emphasize key differences between patients. This may, in turn, better inform patients of the expected changes in speech and swallowing.

The discussion to follow will first address the representativeness of the study sample population with respect to clinico-demographic variables and baseline speech and swallowing outcomes. Next, the discussion will address how speech and swallowing function changed over time for this patient cohort, specifically addressing the return (or lack thereof) of functional status to baseline levels over the first year following cancer treatment. To follow, the associations between clinico-demographic and treatment-related variables and function, as well as possible predictors of function at various time points will be discussed. Finally, the limitations of this investigation will be acknowledged, and clinical implications of this investigation will be presented, along with directions for future research.

4.1 Baseline Characteristics

Based on the clinico-demographic characteristics at baseline, the sample within this study is largely representative of the tongue and FOM cancer population, as other studies have reported similar age at diagnosis, sex ratio, and BMI (Andrade, Antunes, & Durazzo, 2006; Cole et al., 1994; Ihara et al., 2021; Son, Choi, & Kim, 2015). Interestingly, the clinical t-stage of the participants in the current investigation was different compared to what is typically reported in the literature. The most common clinical tumour stage within this investigation was T2 (34 patients; 47.22%). However, other studies of outcomes in patients with tongue and FOM cancer patients typically include patients with more advanced, T4-staged cancers (Andrade, Antunes, & Durazzo, 2006; Cole et al., 1994; Son, Choi, & Kim, 2015). Both speech and swallowing deficits experienced, and overall survival, are often correlated to the TNM staging (Chen, 2019; Costa Bandeira et al., 2008; Ma'aita, 2000; Nicoletti, Soutar, Jackson, Wrench, & Robertson, 2004; Son, Choi & Kim, 2015). As such, the relatively good functional outcomes documented in this patient cohort may reflect the fact that most patients had early-stage tumours; in general, patients with early-stage tumours tend to have better function post-treatment (Gonzalez & March, 2022). It is plausible that our sample population was not representative of advanced, T4-stage tumours (with possible nodal involvement) given that these patients often have high rates of recurrence and poor 5-year survival rates that are in comparison to early-staged T1 and T2 tumours (Ma'aita, 2000). We made an a priori decision to exclude patients who experienced disease recurrence within the first 12 months. This exclusion criterion may have reduced the number of patients with late-stage disease within our sample population; moreover, patients who succumbed to their disease prior to 12-months post-treatment would not be represented in this dataset. Given that the majority of OCCs are diagnosed in advanced stages of the disease (Buelvas & Buelvas, 2010; Montero & Patel, 2015), our results should be applied to the broader population of OCC cautiously.

4.2 Speech and Swallowing Function

4.2.1 Speech Function

It is not often that patients with tongue and/or FOM cancers report pre-treatment alterations in speech performance (Bagan, Sarrion & Jimenez, 2010). However, when speech is evaluated rigorously by S-LPs, speech intelligibility may be impaired even before surgical intervention (Pauloski et al., 1993). In the current investigation, speech performance was not impaired pre-treatment, as determined through clinician ratings using the PSS-HN (Speech) subscale. The speech scores within this investigation were relatively high (close to 100), indicating that the patients were almost always understandable, and that repetition was only occasionally necessary. Our results may differ from previous reports as speech intelligibility was captured differently in this investigation. For example, Pauloski and colleagues assessed speech intelligibility through a conversation sample (1993). Approximately a 350-word speech sample was derived from this conversation, and played for five novice listeners, who then transcribed each word they understand the patient to say (Pauloski et al., 1993). This method may be more sensitive to decreased intelligibility compared to the ‘Understandability of Speech’ subscale of the PSS-HN.

As mentioned in Chapter 1, speech impairments arise early after surgical treatment and commonly persist well beyond the immediate post-surgical period (Eadie et al., 2013; Rinkel et al., 2016; Rodriguez & VanCott, 2005). The results in this investigation revealed that understandability of speech drastically declined immediately post-treatment. This was expected following surgical resection as the tongue plays a crucial role during speech production (Wall et al., 2013). This result is corroborated by a previous study in which patients who experienced tongue resection demonstrated severe impairment in speech intelligibility immediately following surgery (Pauloski et al., 1993).

Similar to the current findings, Lee and colleagues (2014) found that speech function in the long-term (around one-year post-resection), generally recovers (Lee et al., 2014). However, unlike the report by Lee and colleagues, our investigation found that speech function did not return to baseline levels on long-term follow-up. It is important to note that the PSS-HN (Speech) was administered differently in the study by Lee and colleagues (2014); patients were asked via telephone interview to subjectively rate their own intelligibility while the ratings for the current study were clinician-generated. It is important to acknowledge that the patient’s perception of speech function may be different than those of trained clinicians following surgical treatment for OCCs (Constantinescu et al., 2017).

The literature suggests improved speech function, as measured by the PSS-HN (Speech) subscale, is strongly associated with greater time since treatment, implying that speech function may continue to improve over time (Bulbul et al., 2021; Lee et al., 2014).

4.2.2 Swallowing Function

Often, patients with tongue and/or FOM cancers present with pre-treatment swallowing impairments (Gonzalez & March, 2022; Johnson et al., 2020). In particular, dysphagia and odynophagia are the most common symptoms and first signs of OCCs (Gonzalez & March, 2022; Johnson et al., 2020). In the current investigation, oral intake levels were already impaired pre-treatment, which was measured by FOIS and PSS-HN (Diet) subscale scores. On average, patients presented to the clinic eating a total oral diet consisting of multiple consistencies, but with specific food limitations (i.e., avoiding meats and peanuts). Our results do not differ from the literature, as previous studies have also found that these patients were eating a (modified) total oral diet at baseline (Balbinot et al., 2022; Ihara et al., 2021).

As with speech, swallowing impairment occurs early after treatment and is among one of the most frequent long-term side effects of resection, given that important anatomic structures are removed (Bulbul et al., 2020; Hutcheson, 2019; Rinkel et al., 2016). The results of this investigation revealed that, although most patients were still eating a total oral diet, they were requiring special preparations and/or compensations, and eating fewer solid foods and more pureed foods, immediately post-treatment. On the other hand, the level of oral intake differs in the literature, as other researchers have discovered that most patients shift to a tube-dependent diet immediately post-resection (Tseng et al., 2021).

By the long-term time point, patients were still eating a total oral diet with compensations, however eating consistencies similar to those that they were eating at baseline.

This is somewhat consistent with the literature. Most studies have identified dramatic changes in swallowing function immediately post-resection (Balbinot et al., 2022; Pauloski et al., 1993; Yadav et al., 2016). In particular, Pauloski and colleagues (1993) examined swallowing using instrumental assessment (i.e., videofluoroscopy), which revealed that not all patients were able to swallow all consistencies immediately post-treatment (Pauloski et al., 1993). Other studies have also discovered that normalcy of diet tends to return to baseline function over a long-term period (6- to 12-months post-treatment), as most patients return to eating solids at this time point (Lee et al., 2014; Yadav et al., 2016). Within the literature, it is common to see an increase of three or more levels of on the FOIS at long-term follow-up (Balbinot et al., 2022; Tseng et al., 2021).

On average, patients tolerate most solid foods at baseline, then restrict their diet to a soft or liquid diet, and finally return to a "normal" diet with multiple consistencies, including solids by the long-term time point (Lee et al., 2014; Tseng et al., 2021). This investigation differs from other reports in the literature in which significant deterioration in levels of oral intake are common after treatment, but also demonstrate a return to baseline levels (Lee et al., 2014; Tseng et al., 2021; Yadav et al., 2016). On average, patients are reported to tolerate an oral diet pre-treatment, which shifted to a tube dependent diet short-term post-treatment (i.e., immediately and 3-months post-treatment), and finally returned to an oral diet but with limitations long-term post-treatment (6-, 12-, and 24-months post-treatment; Tseng et al., 2021). What differs between this investigation and other studies is that the levels of oral intake were significantly better when compared to other studies, as most patients in this investigation did not require a feeding tube. Additionally, the analyses revealed that patients in this investigation did not return to baseline function by long-term post treatment in this study, whereas other studies found that there was no difference by the long-term (Balbinot et al., 2022; Tseng et al., 2021).

Finally, repeated measures analyses demonstrated that psychosocial swallowing ratings (i.e., PSS-HN (Eat) subscale) were significantly different at the pre- and post-treatment time points. This indicates that psychosocial swallowing did not return to baseline levels by 6- to 12-months post-treatment. In a study by Yadav and colleagues, the authors describe that PSS-HN (Diet) and PSS-HN (Eat) scores go hand-in-hand, as individuals who suffered most with their normalcy of diet, also restricted eating in public to specific places and with specified people because they require special food preparation due to their swallowing deficits (Yadav et al., 2016). This differs from present study in which PSS-HN (Diet) scores returned to baseline levels by the long-term post-treatment time point, whereas PSS-HN (Eat) scores did not. It appears that despite improvements in diet levels, patients in this investigation continued to limit where, and with whom, they would eat.

4.2.3 Dysphagia and QOL

The MDADI did not yield any significant differences when scores were compared across baseline and long-term time points. Some authors found similar results, such that OCC patients demonstrate a significant decrease in MDADI scores one month after treatment, with an upwards trend of recovery, whereby swallowing-related QOL returns back to baseline levels at 12- to 18-months after treatment (Kondo et al., 2019; Tseng et al., 2021). However, other authors have reported significantly poor swallowing-related QOL 24 months after treatment (Tseng et al., 2021). QOL outcomes can be challenging to interpret across studies as these scores are susceptible to the influences of factors beyond physical function. For example, QOL and patient satisfaction (with care) are known to be related, such that dissatisfaction with the health services is associated with negative perception of overall QOL (Asad-Lari, Tamburini, & Gray, 2004).

However, our results are in keeping with the majority of studies that describe return to baseline or near-baseline QOL at 1-year post-treatment.

4.3 Relationships Among Variables of Interest

4.3.1 Relationships Among Clinico-Demographic and Treatment-Related Variables

As outlined in Chapter 1, all HNSCCs are initially staged according to the TNM staging system (AJCC, 2018; Amin et al., 2017; Taibi et al., 2014). Previous research has demonstrated that t-stage and n-stage are significantly associated to each other (Baek, Kim & Ryu, 2015). In the current investigation, there was a moderate positive correlation between (clinical) t-stage and (clinical) n-stage, which was expected (Rosen & Sapra, 2021; Taibi et al., 2014). This relationship suggests that the larger and more invasive the primary tumour, the more regional lymph node involvement. Similar to the expected associations in demographic-related variables, there are expected relationships between the patient-related characteristics of interest.

In this investigation, there were identified correlations that were expected between the patient- and demographic-related variables of interest. For example, the relationship between advancing age and comorbid conditions is well established (Lui & Nguyen, 2018; Saposnik et al., 2008; Yancik et al., 1998). This was consistent with the findings in this investigation, as age at diagnosis and comorbidities, measured by the CCI, were strongly, significantly associated with each other. Not only was this expected because of the results of previous studies, but also because the CCI includes an age-adjustment to include a patient's chronological age (Qu et al., 2020). In general, as age increases, so does the number of comorbid conditions. This is consistent with the literature as there is evidence to support that there is a significant emergence of comorbidities in individuals over the age of 65 years of age (Aslam & Vaezi, 2013; Lui & Nguyen, 2018; Saposnik et al., 2008).

The aim of reconstruction following OCC resections is to maintain the functional integrity of the different structures of the oral cavity for speech and swallowing (Chakrabarti et al., 2015). Studies have found that surgery alone is effective in treating early-staged OCCs and that they usually require minimal reconstruction (Gonzalez & March, 2022; Lo Nigro et al., 2017). On the other hand, advanced staged tumours demand more intense treatment involving reconstruction of the surgical defect (Biron et al., 2017; Gonzalez & March, 2022). As a result, advanced-stage OCCs will usually require the insertion of additional material (i.e., tissue and/or bone) for closure of the primary resection (Malone et al., 2004). In the current investigation, there was a moderate positive correlation between t-stage and reconstruction, corroborating that the higher the t-stage, the more likely the individual will receive reconstruction.

The existing literature presents data which suggests that older adults with HNC are less likely to receive invasive treatment compared to the younger adults because of the array of complications that may arise with older age and age-related comorbidities (Borggreven et al., 2003; Koch et al., 1995; Lee & Kim, 2021). On the other hand, it has also been demonstrated that treatment can be performed safely in the elderly without an increase in complications, particularly if they do not have significant comorbidities (Koch et al., 1995; Lee & Kim, 2021). In this study, age and comorbidities were negatively associated with reconstruction such that older individuals with more comorbidities were less likely to receive reconstruction.

4.3.2 Functional Impact of Patient-, Disease- and Treatment-Related Variables

The impact of advancing age on functional outcomes and QOL following OCC treatment has not been fully explored, and it is still unknown whether age-related changes in speech and swallowing exacerbate functional change post-cancer treatment. Age may be an important predictor of postoperative speech and swallowing function in OCC patients (Fujimoto et al., 2007; Haehl et al., 2020; Tremblay et al., 2019). Yet, the impact of other variables (i.e., comorbidities) has not been studied comprehensively. Therefore, study of potential relationships between clinico-demographic (e.g., age, comorbidities) and treatment-related function post-treatment in patients treated for tongue and/or FOM cancer is of interest.

In addition to the multiple relationships between the clinico-demographic and treatment-related characteristics, there were also significant relationships between these characteristics and functional outcomes. At baseline, only MDADIg scores demonstrated weak, yet positive association with age at diagnosis. In general, the results suggest better perception of overall swallowing-related QOL was significantly associated with age, at baseline. Although the current literature presents inconsistent data on age variations with QOL, one study described that adults over the age of 85 reported having a greater sense of well-being than the younger adults (Stone et al., 2010). Further research proposes that the reason for this inconsistent data is because QOL is a dynamic concept with domains related to physical, emotional, functional and social functioning (Sharma, Mishra & Parikh, 2019), and is often appraised differently across individuals (van Leeuwen et al., 2019). Older adults are more likely to define QOL more positively in terms of promoting and preserving health and well-being (i.e., continuing doing the things they have always done on a day-to-day basis), being satisfied with life, maintaining autonomy and engaging in meaningful social opportunities (Bowling, 2011; van Leeuwen et al., 2019).

There were also significant relationships between adjuvant treatment (i.e., (C)RT) and swallowing function and psychosocial swallowing, as measured by the PSS-HN. In general, the results suggest that if a patient receives adjuvant treatment, then they are more likely to experience swallowing difficulty. There is research to support the benefit in both early and late adjuvant interventions in terms of survival (Charters et al., 2022; Greco et al., 2018; Kraaijenga et al., 2015), but also evidence that highlights the associated substantial side effects that come with intensive treatment, most notably, dysphagia (Kraaijenga et al., 2015). Finally, there were significant relationships between FT duration and psychosocial swallowing function, as measured by the PSS-HN. The results suggest that the longer a patient uses a FT, the more likely they are to experience reduced opportunities to eat with others. The results of this study do not differ from the literature, as other authors have also found similar results that swallowing deficits and withdrawal from social eating contexts could be predicted by length of FT use (Murphy, Ridner, Wells, & Dietrich, 2007; Petersson, Finizia, & Tuomi, 2021; Quon et al., 2015). Generally, long-time FT users are commonly at a higher risk of severe dysphagia (Petersson, Finizia, & Tuomi, 2021; Quon et al., 2015).

4.4 Predictors of Speech and Swallowing Function

Historically, clinico-demographic and treatment-related variables have been presented as independent predictors of speech and swallowing function (Bulbul et al., 2021; Kondo et al., 2017). For example, tumour site, advanced t-stage, and reconstruction status were all found to be important predictors for all PSS-HN subscale scores (Bulbul et al., 2021; Kondo et al., 2017). This investigation sought to determine if there were any clinico-demographic or treatment-related predictors of speech and swallowing function among tongue and/or FOM cancer patients.

In this study, a backwards stepwise multiple linear regression approach was used to determine if any clinico-demographic and treatment-related variables were predictors of speech and swallowing performance among tongue and/or FOM cancer patients (Weigand, 2010). While the regression model examining predictors of long-term PSS-HN (Eat) was significant, and accounted for approximately 46% of the variance, it included multiple independent variables such as CCI scores, t-stage, and adjuvant therapy status. Individuals with more co-existing conditions and advanced t-staged tumours, who have undergone adjuvant treatment, generally scored lower on this subscale suggesting that they usually feel uncomfortable when it comes to eating in public. This could also signify that, because eating is difficult, these patients avoid eating in public. The results in this investigation are similar to a previous study by Kondo and colleagues (2017), in which they described that PSS-HN (Eat) subscale scores can be predicted using t-stage, where in general, advanced t-stage is associated with worse psychosocial swallowing. However, in that study, advanced t-stage had been described as an independent predictor of PSS-HN (Eat) scores (Kondo et al., 2017), rather than as part of a linear combination of independent variables. Kondo and colleagues (2017) also demonstrated that age and degree of reconstruction are other associated, independent predictors of PSS-HN (Eat) scores. The difference in the independent predictors of outcome across studies may be due to the differences in sample size. Kondo and colleagues (2017) used a larger sample size (n = 508) compared to this investigation, which may have helped identify outliers and provide smaller margins of error in the results.

The confirmatory findings within the current investigation can suggest recommendations in relation to real-world applications, from the perspective of both the patient and the clinician.

4.5 Clinical Implications

Based on the primary research questions, this study highlights changes in speech and swallowing function that can be expected following treatment of tongue and FOM cancers. Several components of the results obtained may be of value from a clinical decision-making perspective. Our findings confirm the expected change of speech and swallowing function over time. There was, however, a concerning inability for patients to return to their baseline oral intake level, speech function, and social eating contexts. Novel interventions for persistent speech and swallowing deficits should be the focus of future research. Moreover, it is important to acknowledge that the overall trajectory of speech and swallowing function may be explained by a combination of clinico-demographic and treatment-related variables (i.e., comorbidity, tumour stage, adjuvant therapy) This finding extends the existing literature and prompts researchers to examine the impact of multiple variables related to the health condition, physical functioning, and contextual factors of individual patients when measuring speech and swallowing outcomes.

Within this setting and patient cohort, the absence of statistically significant change over time for swallowing-related QOL could indicate that the current clinical practice is meeting patient needs in terms of emotional, physical and functional aspects of swallowing. However, the utility of QOL measurement in clinical care has not been established (Ihara et al., 2022) such that the continued focus on QOL measurement in clinical care should be probed further. More specifically, there is a lack of data that demonstrates a consistent relationship between QOL and functional outcomes (Ihara et al., 2022; Murphy, Ridner, Wells, & Dietrich, 2007; Yifru, Kisa, Dinegde, & Atanafu, 2021). Although QOL measures can provide useful information to inform clinical decision making in oncology, the subjective nature of these scales makes it difficult for clinicians to interpret scores (Murphy, Ridner, Wells, & Dietrich, 2007). Other measures of outcomes may corroborate whether the perception of improved QOL is related to concomitant functional improvement in speech and swallowing (Murphy, Ridner, Wells, & Dietrich, 2007; Yifru, Kisa, Dinegde, & Atanafu, 2021). The findings in the current investigation suggest that the HN MDT might consider additional measures of outcome, collected at pre-determined time points, to better understand the trajectory of speech and swallowing function. Additionally, the findings suggest that some patients may have benefited from pre-assessment of clinico-demographic and treatment-related characteristics (i.e., age, comorbidities, adjuvant treatment), in order to understand the trajectory of speech and psychosocial swallowing.

Since patients with tongue and/or FOM cancers are living longer post-treatment (Du et al., 2019; Johnson et al., 2020), minimizing the associated toxicities of treatment and decreasing the symptom burden is essential. By understanding how clinico-demographic and treatment-related characteristics impact speech and swallowing performance, and which of these variables have the greatest effect on function, the HN MDT can direct their focus and attention to counselling patients regarding realistic expectations for their health and well-being, based on individual characteristic profiles.

This investigation found that the clinico-demographic and treatment-related variables of interest within this study did not yield any significant independent predictors of speech and swallowing function. However, the combination of these variables (i.e., comorbidities, tumour stage, adjuvant therapy) is able to predict psychosocial swallowing in OCC patients postoperatively. To better inform patients of the expected changes in speech and swallowing function, there should be consideration of a formal assessment for comorbidities, in order to factor them into patient counseling. Additionally, the search for other meaningful predictors of outcome in this patient population should continue.

4.6 Limitations and Directions for Future Research

This investigation employed a retrospective chart review design to evaluate patient functioning using measures prospectively collected in the course of clinical care. We must acknowledge the inherent limitations associated with this type of study design and secondary analysis of data collected for clinical purposes.

4.6.1 Methodology

Retrospective studies allow researchers to utilize existing information to investigate clinically-relevant research questions, often in a more timely and cost-efficient way than can be achieved in prospective cohort studies. However, it is important to acknowledge the limitations associated with the decision to conduct a retrospective chart review. A critical consideration for research that uses a sample population to make claims about a larger population is the process by which participants are selected for study inclusion. Convenience sampling, a method often used in retrospective research, means that the participants were chosen by reviewing medical charts of consecutive patients who presented to the HN MDT during the selected time frame utilizing medical information already available and may have been prone to selection bias. The most rigorous method for preventing selection bias would be to employ random selection (Kahan, Rehal & Cro, 2015). Without random selection, the sample included in this investigation may not be fully representative of the population in question (i.e., patients with tongue/FOM cancer; Gearing et al., 2006). Lack of representativeness often occurs with flawed selection procedures (i.e., sampling bias; Martínez-Mesa et al., 2016). Studies without representativeness may not be a reliable source for drawing conclusions about a target population with a specific level of confidence required for statistical inference (Martínez-Mesa et al., 2016). Within this investigation, there was a lack of representativeness as there were fewer patients with advanced-staged tumours over the study period, which may mean results are challenging to generalize to all oral cancer patients. Further, missing data are more common in retrospective research because routinely collected data is used for different purposes (Altman & Bland, 2007).

4.6.2 Missing Data

Another challenge in utilizing a retrospective study design is the reliance on data collected by others to create a study dataset. Although speech and swallowing data were available at each of the three time points for some patients, it was not the case for the full sample population. In some instances, missing data can be accounted for by variations in the evaluation protocol. For example, in clinical care, not all outcome measures are routinely collected. For example, in the current investigation, the PSS-HN (Eat) subscale and all MDADI subscales could not be included for analysis at the immediate post-treatment time point because these measures were not routinely administered to patients at time of hospital discharge. Additionally, inherent logistical challenges with scheduling patient follow-up appointments at specific time points (6- and 12-month time points) may have resulted in the incomplete dataset. Most studies of functional outcomes in OCC collect data at baseline, and at 3-, 6-, and 12-months post-treatment (Eldridge et al., 2019; Goepfert et al., 2017; Shoji et al., 2014; Tuomi et al., 2020; Xiao et al., 2017; Zuyolam et al., 2021); examination of function immediately post-treatment rarely occurs in research, although it is an important element of clinical care. Researchers have demonstrated that measuring speech and swallowing-related performance immediately post-treatment may not be particularly useful because the decline in function is expected at this time point, and that data at the 3-month post-treatment time point gives more insight on how the patient is functioning post-treatment (Tuomi et al., 2020; Zuyolam et al., 2021). However, the overall theme of post-operative recovery should be understood as a process that extends over a period of time (Allvin, Ehnfors, Rawal & Idvall, 2008). This recovery path ranges from pre-treatment function (which captures the initial disease and its symptoms) to when the patient regains function (Allvin, Ehnfors, Rawal & Idvall, 2008). The immediate post-resection time point is included in the recovery process, as everyday life would have been interrupted by the surgical procedure itself and by the recovery process as a whole (Allvin, Ehnfors, Rawal & Idvall, 2008).

Generally, missing data can be categorized into three types of missing data patterns: missing completely at random (MCAR), missing at random (MAR) and not missing at random (NMAR; Bennett, 2001; Kang, 2013). Some of the data within this investigation can be described as NMAR; as described in Chapter 2, the PSS-HN (Eat) subscale and MDADI scores immediately post-treatment were purposefully excluded because they were not valid measures to collect for patients who are hospitalized. However, all of the other data within this investigation can be described as MCAR because the probability that the data was missing was not related to the specific values nor the set of observed responses (Kang, 2013). Although power may be lost because of MCAR data, the analysis remains unbiased (Kang, 2013). To efficiently handle the MCAR data, it was imperative to select appropriate statistical analyses (i.e., Friedman's Test, Linear Mixed Effects).

It would be biased to suggest a specific methodology that could be applied in future research that would avoid MCAR. Studies surrounding oncology carry a risk relative to missing data, as a wide variety of issues could arise, which could ultimately limit the complete collection of data (e.g., asymptomatic patients requiring less consistent treatment/follow-up, patients foregoing palliative treatment/comfort measures, worsening of symptoms/recurrence requiring adjuvant treatment, high case load demands for the multidisciplinary team, etc.; Bernhard et al., 1998). Future research may collect data prospectively, with a reasonable data collection protocol, in order to mitigate the challenge of missing data. This might require collaboration between researchers and clinicians, as prospective research is not always feasible to be done all by one individual.

4.6.3 Outcome Measures

Patient-reported outcome measures (PROMs) and clinician-rated outcome measures are validated methods of evaluating performance status. Moreover, PROMs permit appraisal of the patient's perspective on a disease and/or treatment that may not be captured by clinician-rated measures, as it relates to a patient's subjective experience of health, QOL, and/or functional status (Weldring & Smith, 2013). PROMs are surrogate markers that often do not capture the underlying physiological impairments of speech and swallowing (Patel et al., 2017). Moreover, impairment-level information is often required to facilitate intervention. In this investigation, we were unable to reliably collect chart data corresponding to impairments in body functions and structure as per the ICF framework (WHO, 2001). However, the patient's subjective experience could be the most important marker of functioning because the psychosocial impairments relative to the disease and its treatment incorporate the patient's perception of how the disease and/or the treatment is affecting their QOL (Patel et al., 2017). Although the utility of PROMs has been established, there are barriers that limit the adoption of PROMs in oncological institutions (Nguyen et al., 2020). Common barriers related to the use of PROMS include the time and independence required to complete these measures, and the perceived irrelevance and lack of value of the PROMs by patients (Duman-Lubberding et al., 2017; Girgis et al., 2017; Kanatas et al., 2009; Trautmann et al., 2016). Incorporating both PROMs and clinical assessment of acoustic and physiological measures where feasible, establishes best practice in oncology (Constantinescu et al., 2017; Gondivkar et al., 2019). For example, the use of a videofluoroscopy as an objective measure to support the findings from the clinician-reported

FOIS scale. Specifically, the extent of impairment that is perceived by patients is not fully explained by clinical tests (i.e., at the level of physiological impairment; Constantinescu et al., 2017; Gondivkar et al., 2019). Implementation of both PROMs and clinical assessments will help inform clinicians in treatment decision making that meets the patient's needs(Gondivkar et al., 2019). Specifically, it will aid in the understanding of the relationship between symptoms and expectations of the trajectory of speech and swallowing function in OCC patients (Gondivkar et al., 2019).

4.6.4 Environmental Factors

The ICF promotes consideration of multiple viewpoints in consideration of health and functioning. Our focus on variables related to the disease and its treatment (health condition), as well as the patient (personal factors), in exploring speech and swallowing function represents a broader exploration of relationships between these various constructs. However, given the lack of consistent reporting of speech and swallowing outcomes at the level of body functions and structures (i.e., articulatory precision, pharyngeal swallow physiology), we were limited to the use of functional outcome measures and a measure of swallowing-related QOL (Figure 1). Future investigations should aim to incorporate evaluation of speech and swallowing at all levels of 'function' to reflect impairments, as well as limitations on activity and participation. Moreover, we were unable to incorporate environmental factors that may have contributed to functioning following OCC treatment. Environmental factors can range from physical factors (e.g., climate, terrain) to social factors (e.g., attitudes, laws), and can act as either barriers to or facilitators of the person's functioning (WHO, 2001). The interaction with environmental factors is an essential aspect of understanding the 'functioning and disability' aspect of the model. In previous studies, it has been established that environmental factors such as geographical regions (and associated sociocultural behaviours), access to care, and treatment facility characteristics, influences one's risk of disease and have been associated with survival outcomes (David et al., 2017; Johnson et al., 2020). However, data related to environmental factors beyond one's geographic residency are not commonly reported in the medical electronic records. This may reflect lack of acknowledgement of the importance of social determinants of health given the predominant biomedical approach to health care provision, or a lack of validated and standardized methods for characterizing aspects of one's environment. Regardless of the reason for the lack of representation of environmental factors in patient charts, attempts to include these factors as variables of interest were precluded by their absence.

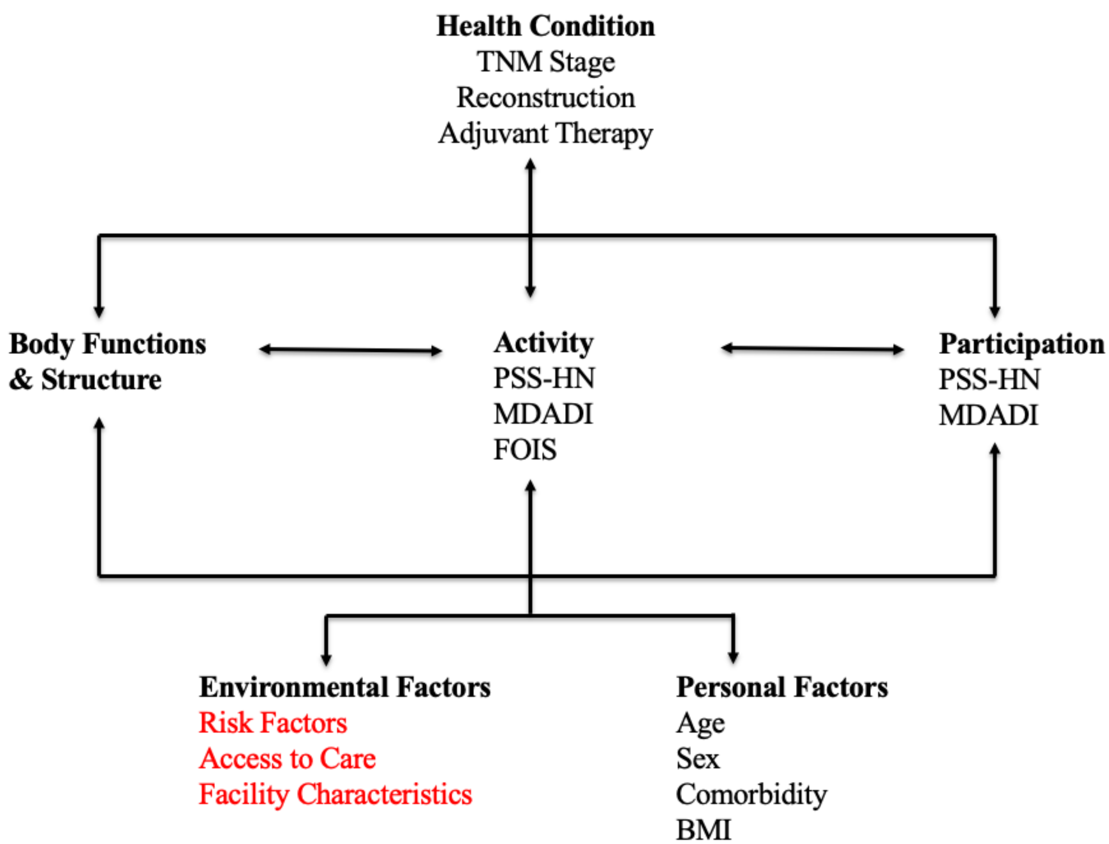
The incidence of HPV-negative HNSCCs does reflect the geographic- and socio-cultural-specific patterns of modifiable risk behaviours, including the use of alcohol, tobacco, chewing tobacco, and areca/betel nut (Johnson et al., 2020; Zhou et al., 2017). For example, the socio-cultural behaviour of chewing areca nut is more common in the South Pacific, and these patients often have the poorest long-term disease-specific survival (Zhou et al., 2017). Variations in geographic- and socio-cultural-specific risk factors can also affect access to healthcare, further impacting function (Dawkins et al., 2020).

Access to and use of healthcare resources are critical to survival outcomes (Chen et al., 2019). Whether an individual has access to these resources, and how they use them, can influence their health behaviour, health outcome, and ultimately QOL (Chen et al., 2019). For example, higher levels of health information access and use are associated with lower levels of smoking and alcohol consumption, the most common etiological risk factors for OCCs (Chen et al., 2019). Multiple barriers create challenges for individuals in rural areas to access and use reliable resources, such as geographical distance and inclement weather (Chen et al., 2019). As such, residents who reside in rural areas have higher all-cause mortality rates and mortality from diseases in compare to urban residents, due to less access and use of preventative health care services (Chen et al., 2019). For example, HNC patients living in rural areas typically experience more mental health issues, and in turn report poorer HNC-specific health-related QOL, in regard to eating post-treatment (Adamowicz et al., 2021). Future research ought to collect information on geographical location, to determine whether there are specific aspects of QOL that are particularly susceptible throughout the patient's survivorship journey in both rural and urban HNC patients.

It has also been established that patients with locally advanced HNSCCs, who are treated with definitive radiotherapy, have significantly improved survival if treated at a high-volume facility (HVF) or at an academic centre compared to lower-volume facilities (David et al., 2017); treatment at an HVF is associated with an approximate 20% improvement in overall survival (David et al., 2017). It has been hypothesized that there are likely a multitude of underlying factors that are driving the improved outcomes and overall survival amongst these patients, including access to ancillary services (i.e., nutrition, palliative care, swallow therapy; David et al., 2017). Future research ought to include instruments that measure aspects of both the social and physical environment as part of the patient's overall survivorship. In Figure 11, we have mapped additional variables of interest onto the ICF framework whose study might further our understanding of the influence of multiple components on one's functioning, disability, and health.

Figure 21

Addition to Variables of Interest



Note. Mapping the variables related to environmental factors to the ICF developed by WHO (2001). Reproduced from International Classification of Functioning, Disability and Health, World Health Organization Geneva, Model of functioning and disability, Page 18, Copyright (2001).

4.7 Conclusion

Research on best treatments for OCC does not routinely consider personal factors (i.e., age and comorbidities), which may result insignificant differences in patient outcomes going unexplained. It is believed that the search to identify the impact of age and other personal factors could help inform patient education and counselling regarding anticipated speech and swallowing outcomes. In particular, the information within this investigation would be helpful in counselling patients prior to OCC treatment regarding the realistic speech and swallowing function trajectory post-resection. In particular, speech and swallowing function did not return to baseline function by 6- to 12-months post-treatment, however QOL ratings did. Additionally, this investigation may prompt different assessment algorithms (i.e., use of different measurement tools) for speech and swallowing function within this population.

The present study investigated the trajectory of speech and swallowing performance, and the relationships between the clinico-demographic and treatment-related characteristics on function post-treatment, with a view to determine predictors of speech and swallowing function post-treatment. Based on prior research, we anticipated that age would be predictive of speech and swallowing function. While it was not an independent predictor, it was predictive when included in measure of comorbidity. To better inform patients of the expected changes in speech and swallowing function, there should be consideration of more formal assessments of comorbidities, in order to factor them into patient counseling. Additionally, the search for other meaningful predictors of outcome in this patient population should continue.

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Appendices

Appendix A

List of Abbreviations

BMI	Body Mass Index
CCI	Charlson Comorbidity Index
CCO	Cancer Care Ontario
COVID-19	Coronavirus 2019
CRT	Chemoradiotherapy
EBV	Epstein Barr Virus
EORTC-QLQ	European Organization for Research and Treatment of Cancer Quality of Life Questionnaire
FOIS	Functional Oral Intake Scale
FOM	Floor of Mouth
FT	Feeding Tube
HN MDT	Head and Neck Multidisciplinary Team
HNC	Head and Neck Cancer
HNSCC	Head and Neck Squamous Cell Carcinoma
HPV	Human Papillomavirus
HVF	High-Volume Facility
ICF	International Classification of Functioning, Disability, and Health
KPS	Karnofsky Performance Scale
LME	Linear Mixed Effects

LRCP	London Regional Cancer Program
MAR	Missing at Random
MCAR	Missing Completely at Random
MDADI	M. D. Anderson Dysphagia Inventory
MDADIc	MDADI Composite Subscale
MDADIe	MDADI Emotional Subscale
MDADIf	MDADI Functional Subscale
MDADIg	MDADI Global Subscale
MDADIp	MDADI Physical Subscale
NCCN	National Comprehensive Cancer Network
NMAR	Not Missing at Random
OCC	Oral Cavity Cancer
OPSCC	Oropharyngeal Squamous Cell Carcinoma
PSS-HN	Performance Status Scale – Head and Neck
PROM	Patient-Reported Outcome Measure
QLQ-H&N35	Quality of Life Questionnaire - Head and Neck Module
QOL	Quality of Life
RT	Radiotherapy
S-LP	Speech Language Pathologist
SCC	Squamous Cell Carcinoma
SD	Standard Deviation
WHO	World Health Organization

Appendix B

Ethics Approval

Date: 11 April 2022

To: Dr. Julie Theurer

Project ID: 119764

Study Title: Exploring functional and quality of life outcomes in patients with cancers of the upper aerodigestive tract and esophagus

Application Type: HSREB Initial Application

Review Type: Delegated

Full Board Reporting Date: 26/April/2022

Date Approval Issued: 11/Apr/2022

REB Approval Expiry Date: 11/Apr/2023

Dear Dr. Julie Theurer

The Western University Health Science Research Ethics Board (HSREB) has reviewed and approved the above mentioned study as described in the WREM application form, as of the HSREB Initial Approval Date noted above. This research study is to be conducted by the investigator noted above. **All other required institutional approvals and mandated training must also be obtained prior to the conduct of the study**.

Documents Approved:

Document Name	Document Type	Document Date	Document Version
119764_Research Protocol_v1_2022Feb18	Protocol	18/Feb/2022	1.0
Data Collection Form v1 2022Feb18	Other Data Collection Instruments	18/Feb/2022	1.0

No deviations from, or changes to, the protocol or WREM application should be initiated without prior written approval of an appropriate amendment from Western HSREB , except when necessary to eliminate immediate hazard(s) to study participants or when the change(s) involves only administrative or logistical aspects of the trial.

REB members involved in the research project do not participate in the review, discussion or decision.

The Western University HSREB operates in compliance with, and is constituted in accordance with, the requirements of the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans (TCPS 2); the International Conference on Harmonisation Good Clinical Practice Consolidated Guideline (ICH GCP); Part C, Division 5 of the Food and Drug Regulations; Part 4 of the Natural Health Products Regulations; Part 3 of the Medical Devices Regulations and the provisions of the Ontario Personal Health Information Protection Act (PHIPA 2004) and its applicable regulations. The HSREB is registered with the U.S. Department of Health & Human Services under the IRB registration number IRB 00000940.

Please do not hesitate to contact us if you have any questions. Sincerely,

[redacted]

Note: This correspondence includes an electronic signature (validation and approval via an online system that is compliant with all regulations).

Page 1 of 1

Curriculum Vitae

Victoria Lebedeva, B.HSc., M.Sc. Candidate

Education

The University of Western Ontario **2020 – Present**

Master of Science in Health and Rehabilitation Sciences

The University of Western Ontario **2016 – 2020**

Bachelor of Health Sciences, Honours Specialization in Rehabilitation Sciences

Related Work Experience

Graduate Research Assistant **2020 – Present**

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Awards and Achievements

Teaching Assistant Award, *The University of Western Ontario* **2021 – 2022**

Dean's Honour List, *The University of Western Ontario* **2019 – 2020**

Research Projects and Presentations

Lebedeva, V. & Theurer, J. Speech and Swallowing Outcomes After Tongue and/or Floor of Mouth Cancer Surgery. 2022.

"Speech and Swallowing Performance in Patients with Oral Cavity Cancer". 31st Annual Meeting of the Dysphagia Research Society. San Francisco, California. March 16 2023.

"The Effect of Age on Swallowing Outcomes after Head and Neck Cancer Surgery". LHSC Head and Neck Otolaryngology Research Meetings Presentation. London, ON. April 15, 2021.

“The Effect of Age on Swallowing Outcomes after Head and Neck Cancer Surgery”. The University of Western Ontario: Speech and Language Sciences Seminar Presentation. London, ON. February 2, 2021.