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EFFECTIVENESS OF PROPHYLACTIC LINGUAL STRENGTHENING EXERCISES FOR PATIENTS WITH HEAD AND NECK CANCER A SYSTEMATIC REVIEW

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EFFECTIVENESS OF PROPHYLACTIC LINGUAL STRENGTHENING EXERCISES FOR PATIENTS WITH HEAD AND NECK CANCER

A SYSTEMATIC REVIEW

THESIS

A thesis submitted in partial fulfillment of the
requirements for the degree of Master of Science in
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at the University of Kentucky

By

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ABSTRACT OF THESIS

EFFECTIVENESS OF PROPHYLACTIC LINGUAL STRENGTHENING EXERCISES FOR PATIENTS WITH HEAD AND NECK CANCER A SYSTEMATIC REVIEW

Radiation treatment for head and neck cancer has devastating effects on swallowing ability. Prophylactic swallowing exercises are often recommended. However, the evidence for these exercises is equivocal and information regarding critical components of an exercise program is lacking. The purpose of this systematic review was to examine the evidence regarding lingual strengthening exercises as a component of a prophylactic swallowing program.

KEYWORDS: Head and neck cancer, Dysphagia, Prophylactic Swallowing Intervention, Organ Preservation Treatment

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04/24/2019
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CHAPTER 1. INTRODUCTION

1.1 Introduction

Approximately 38.4% of men and women will be diagnosed with cancer at some point during their lifetimes. (National Cancer Institute, 2019) In 2018 alone, an estimated 1,735,350 new cases of cancer were diagnosed in the United States and 609,640 people died from the disease. (National Cancer Institute, 2019) In the United States, head and neck cancer (HNC) comprises an estimated 3% of these cases, with approximately 63,000 Americans developing head and neck malignancies annually (ASHA, 2019) Head and neck malignancies may present at various anatomic sites in the region including the oral cavity/pharynx, larynx, nasopharynx, nasal cavity/paranasal sinus, and hypopharynx. (ASHA, 2019) Different types of cancer are associated with each anatomical site; cancer types behave and progress differently. The most common type of head and neck cancer across subsites (excluding the nasopharynx) is squamous cell carcinoma (SCC).(National Cancer Institute, 2019)

Historically, tobacco and alcohol use have been identified as primary risk factors for head and neck SCC (HNSCC). (National Cancer Institute, 2019) Individuals who use both tobacco and alcohol have a significantly greater risk of malignancy than individuals who just use one or neither product. (National Cancer Institute, 2019) More recently, an increasing number of cases of HNC are being linked to the human papilloma virus (HPV), a grouping of more than 150 related viruses transmitted through sexual contact. (American Cancer Society, 2019) HPV-16 has been linked to an estimated 30,000 oropharyngeal cancers and 25% of head and neck squamous cell carcinomas (HNSCC) globally each year. (American Cancer Society, 2019) The most common HPV positive HNSCC sites are tonsillar and base of tongue, but it has also been detected in a subset of laryngeal and oral cavity malignancies in several studies. (D’Souza & Dempsey, 2011)

The epidemiology of SCC has been evolving over the past few decades. (D’Souza & Dempsey, 2011) As the use of tobacco has decreased nationwide, so have the cases of HPV-negative/tobacco-associated cancers. (American Cancer Society, 2019) In contrast, the occurrence of HPV-positive oropharyngeal cancer is on the rise. (D’Souza & Dempsey, 2011) Fortunately, although more common, HPV-positive cancer has been linked to younger patients and better survival outcomes. (D’Souza & Dempsey, 2011) The three-year survival rate of HPV-positive HNSCC is 84% in contrast to a significantly lower rate with HPV-negative cases at 57%. (D’Souza & Dempsey, 2011) The National Cancer Institute’s Surveillance, Epidemiology, and End Results (SEER) Program reported superior long-term survival rates as well, with a median of 131 months post-treatment for HPV-positive patients versus 20 months in HPV-negative patients. (D’Souza & Dempsey, 2011) With growing survival rates, the number of patients requiring treatment and rehabilitation is on the rise, making this a primary medical concern for medical professionals and patients alike.

Regardless of site, type of cancer, etiology, and corresponding survival rate, patients with HNC are recommended to undergo oncology treatment, which may be palliative or curative. Treatment is tailored to the patient’s needs. Site and stage of the cancer, patient history and current health, and doctor experience are factors that contribute to the treatment selection. (National Cancer Institute, 2019) Today, surgical resection, with or without radiotherapy, and chemotherapy with or without radiation, also known as organ preservation treatment, are common curative options for patients. (Lazarus, 2006)

Formerly, HNC was managed with open surgery, with or without postoperative radiotherapy. (Nichols et al., 2013) Traditional open transcervical and mandibulotomy exposure techniques as well as transection and/or removal of critical swallowing musculature were common practices. (Nichols et al., 2013) The approach effectively controlled tumors, but, the speech, swallowing, and cosmetic outcomes were poor. High rates of complication lead to organ preservation techniques, influencing centers to opt more often for radiation treatment, reserving surgical resections to those individuals requiring salvage intervention. (Nichols et al., 2013) More recently, first-line management of HNC has involved chemoradiation therapy (CRT), as research demonstrates comparable survival outcomes to open surgery, with significantly decreased morbidity. However, current findings suggest that sparing the organs from surgical resection does not guarantee preservation of their function. (Nichols et al., 2013)

Adverse effects of CRT are often long-lasting and may manifest acutely or longitudinally after the cessation of treatment, known as late radiation effects. (Nichols et al., 2013) Common toxicities include dysphagia (swallow dysfunction), mucositis (inflammation and ulceration of mucous membranes), xerostomia (dry mouth), fibrosis (thickening and scarring of tissue), osteoradionecrosis (bone death due to radiation), neutropenia (decreased white blood cell count), neurotoxicity (adverse effect on central or peripheral nervous system), nephrotoxicity (adverse effect on kidneys), and ototoxicity (adverse effect to inner ear). Dysphagia, an impairment of the swallow, is among the most commonly cited functional impairments for oropharyngeal cancer survivors. (Hutcheson et al., 2013)

Dysphagia presents in the HNC population as a consequence of the tumor altering bolus flow and anatomical motility or the damaging effects of oncologic treatment. Irradiated structures become fibrotic and develop scar tissue over time; impairing their movement and coordination. (Lazarus, 2006) When reviewing the literature, most patients with head and neck cancer presented with reduced tongue strength, increased oropharyngeal transit times, reduced tongue base retraction, impaired epiglottic inversion, decreased laryngeal elevation, and trismus. Additionally, due to sensory impairments, impaired bolus control, and oropharyngeal residue many patients are at risk for aspiration pneumonia. (Lazarus, 2006) As a result, many patients are candidates for alternative means of nutrition, and begin to use a PEG tube as their primary source of nutrition. (Vivrani et al., 2015) Without the usual load on the swallowing mechanism, atrophy may occur, exacerbating the effects of radiation-associated edema and fibrosis. (Hutcheson et al., 2013)

Reduction in lingual strength has been documented in multiple studies, likely due to lingual tissue fibrosis in later stages. (Sanfilippo & Lazarus, 2010) Logemann and colleagues found lingual weakness to be one of the most common disorders at baseline and 3 months after treatment. (53) Lazarus and colleagues reported similar findings, as they determined significant reduction in tongue strength from baseline to 3- and 6-months post-treatment for patients treated with CRT. (Lazarus et al., 2017)

Physiologic signs of lingual weakness include increased oral, base of tongue, and pharyngeal residue, prolonged oral preparatory and transit times; and reduced efficiency of the oropharyngeal swallow. (Wilson & Green, 2006) These difficulties can be present even when the tongue is able to make full contact with the palate, suggesting swallowing difficulties are possible even with normal lingual range of motion. (21) Beyond physiologic changes in the swallow, tongue strength can directly affect quality of life. Patients commonly report extended meal times due to slowed mastication, increased efforts to control the bolus, and the fear of choking.

Speech-language pathologists (SLPs) are part of a multidisciplinary team including the medical oncologist, radiologist, maxillofacial prosthodontist, social worker (or psychiatrist), physical therapist, nutritionist, and oncology nurse that assist patients with a new cancer diagnosis. (Lazarus, 2000) Meetings with the team are conducted to ensure patient understanding of treatment options and post-treatment outcomes. (Lazarus, 2000) The SLP counsels the patient about specific communication (voice and speech) and swallowing outcomes that correspond to the chosen oncology treatment methods. (Lazarus, 2000) These counseling sessions may have to be done over the phone, but meetings before surgery or at/ before chemotherapy or radiation treatments are most beneficial. (Lazarus, 2000)

SLPs recommend dysphagia evaluations before initiation of, immediately post-, and longitudinally post-CRT to monitor swallow safety and the need for/effects of dysphagia intervention. (Lazarus, 2000) Due to a mixed body of literature, some SLPs elect to initiate swallow exercises prophylactically, at the initiation of RT/CRT, while others choose to treat dysphagia reactively, and begin post-RT/CRT or when novel swallowing dysfunction presents during treatment. (Lazarus, 2000) Regardless of the timing, management of dysphagia includes evaluating need for diet modification, compensatory strategies during mealtimes to improve diet tolerance, or rehabilitation exercises to maintain or improve the swallow. SLPs also provide education related to oral hygiene to prevent further risk of aspiration pneumonia. Multiple interactions with the patient may be necessary to ensure comprehension and adherence. (Lazarus, 2000)

Prophylactic exercises are a set of exercises given to the patient to complete throughout and after cancer treatment that may target range of motion or strengthening of the tongue, jaw, or pharyngeal muscles. The goal of a preventative approach is to encourage patients to continue use of their swallowing mechanism, as many patients stop eating and drinking by mouth due to toxicities of treatment. Disuse of the system can lead to muscular atrophy, furthering the severity of dysphagia. Exercises are suggested to lessen the impact of functional decline and support swallowing musculature proactively. (Hutcheson et al., 2013)

Although they are commonly recommended in clinical practice, literature surrounding prophylactic swallowing protocols is limited and equivocal. Significant methodological differences exist amongst published studies. For example, the chosen behavioral interventions for prophylactic studies continue to vary greatly. Of the 20 studies reviewed by Greco and colleagues, range of motion was targeted in 19, with 13 utilizing the Mendelsohn maneuver, 14 targeting the tongue, and 10 targeting the jaw. Strengthening exercises were used in 17 studies with 12 utilizing the effortful swallow, 8 targeting the tongue, and 4 targeting the jaw. Four studies included compensatory strategies along with the exercises. Dosages, outcome measures, and timing of measures also varied in each of these studies. Further, studies that reported on lack of adherence, suggested it was a significant concern.

A number of studies demonstrate at least one significant benefit of prophylactic exercises. Hutcheson and Lewin conducted a review finding treatment groups with superior swallowing-related quality-of-life scores, improved base of tongue retraction and epiglottic inversion, larger post-radiotherapy muscle mass (genioglossus, mylohyoid, and hyoglossus) and T2 signal intensity on magnetic resonance imaging, and shorter duration of gastrostomy dependence after radiotherapy. (Hutcheson & Lewin, 2012) Despite this, other studies report limited to no benefit in one or more outcome areas, such as a random controlled trial conducted by Mortensen et al. (2015).

The current studies have been conducted with heterogenous groups of participants, with each agency providing a different exercise protocol, and assessing with a variety outcome measures, often not representative of the physiologic, quality of life, and functional domains. Although preventative treatment is commonly recommended in clinical practice, literature surrounding these protocols is limited and equivocal. Further research is necessary to determine what exercises, if any, should be included within a prophylactic swallowing intervention protocol.

1.2 Statement of the Problem

Dysphagia commonly develops as a primary complication of head and neck tumor or as a result of oncologic treatment. (Vivrani et al., 2015) Evidence suggests functional changes in swallow may be partially attributed to lack of lingual strength and control. Exercises targeting lingual strength have been found to result in improved swallow function. However, lingual strengthening exercises are not always included as a part of prophylactically or reactively administered protocols. Prophylactic swallowing exercises have shown to improve functional swallowing outcomes, but determining specific benefits is difficult due to lack of consistent exercise protocol and outcome measures. A swallowing protocol for HNC patients must be defined with the following tenants: timing of initiation in relation to oncologic treatment, specific exercises included, and dosage of exercises including repetitions, cycles, and duration. Later research endeavors may seek to establish individualized prophylactic exercise protocols for specific subsites of HNC. Established protocols must be both effective and feasible for patients to complete, as patient adherence has been a concern in published studies.

1.3 Purpose of Study

The purpose of this study was to investigate the evidence for a lingual strengthening component in a prophylactic swallowing protocol for head and neck cancer patients undergoing primary chemoradiation therapy. A systematic review was conducted to review studies with prophylactic swallowing interventions for HNC patients specifically with an oral-tongue strengthening component without concomitant lingual range of motion exercises. This study aims to differentially examine the evidence and to gather important information that may improve future interventions. Previous systematic reviews have not isolated literature pertinent to prophylactic swallowing exercises for HNC patients with a lingual component. Several studies initiated reactive intervention or only served an observational role by collecting immediately acute and longitudinal post-treatment data. Further, research specific to lingual strengthening intervention for patients treated with primary CRT is lacking. Many studies focus on base of tongue retraction or pharyngeal wall exercises while others target oral tongue range of motion without a strengthening component. Existing studies targeting lingual weakness include patients that undergo surgical intervention (e.g. TORS) that can impact the gross anatomy of the tongue contributing further to the heterogeneity of the HNC population.

CHAPTER 2. LITERATURE REVIEW

2.1 Head and Neck Cancers

Head and neck cancers are categorized into anatomic areas, based on the location in which they originate: oral cavity, pharynx, larynx, paranasal sinuses, nasal cavity, and salivary glands. Each area is prone to different types and severities of cancer, impacting survival rates, physiologic deficits, and quality of life.

More than 90% of head and neck cancers arise from dysplasia in the squamous cells of epithelium within oral cavity, oropharynx, and larynx. (National Cancer Institute, 2019) Defining the anatomical borders of these subsites highlights the complexity of the region. The SEER Summary Staging Manual defines the oral cavity as extending "from the skin-vermilion junction of the lips to the junction of the hard and soft palate above and to the line of circumvallate papillae below". (National Cancer Institute, 2019) The oral pharynx is labeled as the "portion of the continuity of the pharynx extending from the plane of the inferior surface of the soft palate to the plane of the superior surface of the hyoid bone (or floor of the vallecula) and includes the base of tongue, inferior surface of the soft palate and the uvula, the anterior and posterior tonsillar pillars, the glossotonsillar sulci, the pharyngeal tonsils, and the lateral and posterior walls." The anterior boundary is the "lingual surface of the suprahyoid epiglottis, thyrohyoid membrane, the anterior commissure, and the anterior wall of the subglottic region, which is composed of the thyroid cartilage, the cricothyroid membrane, and the anterior arch of the cricoid cartilage." (National Cancer Institute, 2019) Posterior lateral limits include the "aryepiglottic folds, the arytenoid region, the interarytenoid space, and the posterior surface of the subglottic space represented by the mucous membrane covering the cricoid cartilage." (National

Cancer Institute, 2019) Superior lateral limits are “bounded by the tip and the lateral border of the epiglottis”. (National Cancer Institute, 2019) “A plane passing through the inferior edge of the cricoid cartilage” bounds the inferior limits. (National Cancer Institute, 2019) The described oral, oropharyngeal, and laryngeal structures partially contribute to the many systems of the body: digestive, respiratory, nervous, or endocrine. Deficits within any of these components may impact the physiology of the systems as a whole. (National Cancer Institute, 2019) More specifically, malignant or oncology treatment-related changes in these three cavities impact the motoric ability and sensory response required to prepare and transport a bolus efficiently and safely, resulting in one of the most common and potentially life-threatening consequences of HNC: dysphagia. (National Cancer Institute, 2019)

2.2 Oncology Treatment Effects

Primary treatment options for patients with HNC include surgical intervention, radiation, chemotherapy or a combination of approaches. Radiation therapy uses x-rays to shrink tumors and kill cancer cells. It can be administered as external-beam, which contacts the tumor and surrounding areas or as internal radiation therapy, which places radioactive pellets or rods into the cancer site. Chemotherapy is a powerful medication taken orally, intravenously, or by injection that can be used to palliate symptoms or in conjunction with surgery or radiation therapy to eliminate cancer cells. Each treatment option is accompanied by different side effects and toxicities for the body; when treatment options are combined, the risk and severity for those side effects increases.

Radiation restricts the reproductive potential of both healthy and malignant cells, and results in cell death. A newer form of external beam radiotherapy, intensity modulated radiation therapy (IMRT), has been developed in attempts to impact less healthy tissue, and produce fewer side effects. (Strojan et al., 2017) However, adjacent cells continue to be affected. Unfortunately, cells adjacent to HNC malignancies are commonly a component of the swallowing mechanism and toxicity cannot be avoided. (Strojan et al., 2017)

All patients with HNC treated with RT are at high risk of oral complications, despite the anatomic subsite of their malignancy. (Sroussi et al., 2017) The acute effects of RT include mucositis, thickened secretions, mucosal infections (such as oropharyngeal candidiasis), general pain, and sensory disruptions. (Sroussi et al., 2017) The long-term chronic effects of head and neck RT include tissue fibrosis and necrosis, salivary gland dysfunction, increased susceptibility to mucosal infections, neuropathic pain, sensory disorders, and an increased susceptibility to dental caries and periodontal disease. (Sroussi et al., 2017) These oral complications may contribute to or exacerbate symptoms of dysphagia.

The swallow involves complex coordination between structures of the brain, corresponding cranial nerves, muscles, and sensory receptors; radiation can disrupt the anatomy at any stage of the circuit. (Strojan et al., 2017) As such, post radiation swallow function may be impaired due to a number of reasons including neuropathy, edema, fibrosis, and atrophy. (61)

Although it is well known that radiation negatively impacts the functional swallow, there have been very few studies investigating the fibrotic effect of radiation on the swallowing mechanism. (Lazarus, 2006) In part, this may be because studying lingual, laryngeal, and pharyngeal muscle tissue in the animal model is much less challenging. Much of the research examining post-radiation fibrosis focuses on skeletal muscles, specifically limbs; where up to 25% of strength can be lost following RT. (Lazarus et al., 2000) The decline in musculature strength post-RT may be result of impaired neural transmission, impaired musculature contraction, fewer muscle fibers and reduced fiber size, or replacement of muscle with connective and fibrotic tissue, due to reduced blood supply in the muscle. Tongue strength and endurance could be impacted in the same way. (Lazarus et al., 2000) Hypothesized rigidity from late-onset fibrosis could further compromise the weakened lingual structures, resulting in profound movement and strength impairment for deglutition. (40,48)

Compressive fibrosis and/or direct ischemic nerve damage has been linked to radiation-associated lower cranial nerve palsy. Evidence for rarely-occurring, cranial neuropathy is limited, but existing studies are concentrated to nasopharyngeal cancers (NPC). (Hutcheson et al., 2017) However, recent case reports suggest non-NPC HNC survivors may be at risk for progressing polyneuropathies, damage effecting peripheral nerves, and denervation, loss of nerve supply impeding physiologic function, due to lower cranial nerve palsy in long-term survivorship. (Hutcheson et al., 2017) Cranial nerves IX, X, and XII, have been specifically studied due to their known involvement with the pharyngeal swallow.(Hutcheson et al., 2017) A study by Hutcheson and colleagues determined that 3 of 59 patients developed delayed hypoglossal palsy on the same side as their IMRT-treated tumor.(Hutcheson et al., 2017) In a cohort of 387, hypoglossal palsy was also diagnosed post-radiotherapy in 17 participants with nasopharyngeal carcinoma. (King et al., 1999) The hypoglossal nerve innervates 3 of the 4 paired extrinsic muscles of the tongue: genioglossus, hyoglossus, styloglossus. (Learned et al., 2012) Damage to this nerve produces characteristic clinical manifestations, including unilateral atrophy of the tongue musculature. (Learned et al., 2012)

Due to the complex neuromuscular involvement, lingual discoordination and atrophy are two of the most commonly reported symptoms dysphagia post-C/RT. (Wilson & Green, 2006) In the oral phases, reduced lingual strength and endurance may present as inefficient bolus preparation (collecting food/liquid into a cohesive ball), difficulty propelling the bolus into the oropharynx (forcing the bolus against the palate and posteriorly), and increased oral residue (e.g. on tongue surface, anterior and lateral floor of the mouth, and hard and soft palate). (Lazarus et al., 2000) Xerostomia and painful mucositis further the patient's difficulty, causing oral preparation of the bolus to be laborious and uncomfortable. These factors may limit oral intake, putting patients at risk for malnutrition (with weight loss) and dehydration. (Vivrani et al., 2015)

Oral or pharyngeal residue, possibly secondary to oral or base of tongue weakness, places a patient at risk for aspiration after the swallow. This risk is heightened due to a link between radiation and laryngeal sensory impairment. (Xu et al., 2015) Without any overt responses to aspiration (coughing, choking, etc), many silent aspirators are undetected, resulting in under-identified and under-reported cases. (Xu et al., 2015) Prolonged aspiration without intervention, coupled with limited ambulation increases risk for developing aspiration pneumonia. In a recent study, Xu and colleagues (2014), found that 801 of 3513 HNC patients identified between 2000-2009 developed aspiration pneumonia at a median of five months after treatment initiation. Of those patients, 674 were hospitalized with 301 in intensive care units, and the 30-day mortality rate was 32.5%. (Xu et al., 2015)

Due to the previously described consequences of treatment, PEG tubes may be placed prophylactically to ensure that patients are able to receive adequate nutrition during their oncology treatment. Some patients and care teams choose to place a PEG reactively, should the need arise. (Vivrani et al., 2015) In a recent literature review by Locher and colleagues, "feeding tube dependence rates of 4% to 18.7% before the initiation of RT/chemotherapy, 29.6% to 40.8% during treatment, 40% to 45% at 3 months, and 8% to 60% at 12 months post-RT/chemotherapy" were reported. (Vivrani et al., 2015) It is to be noted that PEG use does not completely remove the risk for aspiration pneumonia, as refluxed stomach contents and saliva can still be aspirated. Further, limiting oral intake (PO) during oncologic treatment, through patient non-adherence to diet modification, general discomfort during swallow, lack of appetite due to nausea, or PEG tube dependence, can pose a risk for HNC patients by promoting atrophy of the swallowing mechanism. (Hutcheson et al., 2013)

2.3 Survivorship and Quality of Life

The most critical outcome for a patient is cure, but with a positive trend in survival rates, quality of life (QOL) in post-treatment phases has become a forefront issue in head and neck oncology. (Ringash, 2015) QOL combines the person's perspective of their physical health, psychosocial state, independence, their relationships, and overall well-being. It may evolve throughout the identified phases of survival: acute (initial treatment), extended (recovery and adaptation to a new normal) and permanent (long term) periods. (Ringash, 2015) Healthcare providers are able to care for patients with HNC through multiple phases, as oncology teams encourage routine follow-ups with patients up to 5 years post-treatment. (Ringash, 2015) During this time, QOL can be measured using multiterm and multi-domain questionnaires to develop objective scores for a patient profile. (Ringash, 2015)

Decline in QOL is common for patients with HNC, regardless of the mode of treatment or stage of survivorship, due to a combination of advanced disease and early/late effects of aggressive treatment modalities. (Ringash, 2015) According to a study conducted by Lin and colleagues, patients with HNC experience one of the highest rates of depression, of oncology patients, at 44%. (Lin, Starmer, & Gourin, 2012) This study found depressive symptoms continued to be present at 1 year following treatment oncology treatment and associated these symptoms with subjective swallowing impairment and reduced QOL. (Lin, Starmer, & Gourin, 2012)

Within this population, patients diagnosed with dysphagia have been reported to experience significantly decreased QOL in comparison than those without swallow dysfunction. (Garcia-Peris et al., 2007) Dysphagia has been correlated with physical and emotional challenges, as it presents additional health risks for patients and impacts dining as a social activity. Although modifications can be made for patients to eat something safely or utilize an alternative means of nutrition, mealtimes are altered from the norm. A study by Garcia-Peris and colleagues reported that 62% of patients avoided eating with others and approximately 37% of patients felt embarrassed at mealtimes. Furthering a sense of isolation, family and friends may feel reluctant to eat meals around a patient who has a modified diet, uses compensatory strategies during their meal, or faces frustration while eating. Patients or caregivers may also experience burden due to extensive preparation of modified diets or alternate means of nutrition, resulting in psychosocial consequence or nonadherence for the patient.

2.4 Timing of Dysphagia Intervention

When taking into consideration the significant impact that dysphagia can have on a survivor of HNC, intervention strategies should be carefully selected in attempts to provide the most comprehensive, effective care possible to improve swallow function and by extension, QOL. Dysphagia intervention can be delivered to the patients through one of three models: an educational/monitoring model, a reactive model, and a prophylactic model. The traditional model is reactive management, only treating patients if dysphagia persists post-RT/CRT; however, this model lacks patient counseling and education. (Vivrani et al., 2015) The educational model was initiated in the 1990s and involved baseline swallow evaluation, educating the patient about swallow changes during oncologic treatment, monitoring swallow function throughout treatment, and referring if alternate means of nutrition was indicated. (Vivrani et al., 2015) Recently, prophylactic intervention has been the preferred service delivery model, providing patients with education before initiating RT/CRT and exercises/strategies for the duration of oncologic treatment. With this model, swallow status is typically evaluated at baseline, at conclusion of RT/CRT, and longitudinally. (Vivrani et al., 2015)

2.4.1 Prophylactic Administration

While most studies support the use of prophylactic swallowing protocols, an established intervention protocol with comprehensive, consistent outcome measures has yet to be determined. (Krisciunas et al., 2012) Similar to the intervention programs described in published studies, in clinical practice, prescribed exercises and dosage varies by agency. Roe and colleagues conducted a web-based survey in the United Kingdom investigating the current trends in dysphagia assessment and intervention for patients with HNC receiving radiotherapy. (Roe et al., 2011) Of the 42 teams completing the survey, 71.4% administered prophylactic treatment, but protocols demonstrated difference in types of exercise, intensity, and duration. (Roe et al., 2011) According to the survey, the most common types of exercises included in prophylactic swallowing protocols include those targeting oral tongue ROM and strength, hyolaryngeal movement, upper esophageal sphincter opening, and tongue base ROM and strength. (Roe et al., 2011) Less commonly prescribed exercises targeted stretching of the jaw, neck, facial muscles, and lips. The super-supraglottic swallow and supraglottic swallow least commonly prescribed. (Roe et al., 2011) Prescribed dosage varied significantly with 36.1% of teams recommending patients perform their exercises five times per day; 19.4% prescribed their exercises three times per day; 5.5% recommended that patients do their exercises twice per day; 2.8% prescribed exercises once per day; and 25% of teams recommended that patients perform their exercises as much as possible. (Roe et al., 2011) A similar study was completed in the United States by Krisciunas and colleagues revealing, 46.9% of SLPs provide intervention only after dysphagia symptoms developed post-RT compared to only 18.3 % who intervened proactively. (Krisciunaset al., 2012) The survey indicated that the majority of SLPs prescribe therapy 7 days/week and 10–20 min/day for the dysphagic patient, while approximately 25%of SLPs choose to prescribe therapy 4–6 days/week and 30+ min/day. (Krisciunaset al., 2012)

Although there is inconclusive evidence concerning which exercises to include in a prophylactic swallowing protocol, some studies have suggested simply maintaining use of the swallowing mechanism during radiation is important. A recent study by Hutcheson and colleagues, found that patients who either follow oral diets or exercise through RT/CRT have better outcomes than those who do not, but swallowing outcomes are best among patients who both eat and exercise. (Hutcheson et al., 2013) With that, use of the swallowing mechanism has been suggested to reduce muscle atrophy and prevent decline in oropharyngeal swallow efficiency. This suggests that a preventative approach may have potential to consistently benefit patients if the appropriate components are selected for inclusion.

2.5 Types of Exercises Included in Intervention

There are two broad categories of dysphagia intervention that may be included within a protocol: compensatory strategies and rehabilitative strategies. The effectiveness and appropriateness of each varies depending on the patient's swallow function, overall health, and cognition. (Logemann & Larsen, 2012) Compensatory strategies, strategies that are only effective when used, include postural changes, manipulating bolus characteristics, and swallowing maneuvers. Rehabilitative exercises (sometimes referred to as restorative) are intended to improve swallowing physiology, and over time, minimize impairment. (Pauloski, 2008) Examples of rehabilitative exercises include those that target range of motion, coordination, and/or strength of oral, pharyngeal, or laryngeal structures. Rehabilitative exercises best match the physiologic needs of RT/CRT recipients. (Pauloski, 2008)

2.6 Lingual Strengthening Intervention

The tongue serves a primary role in the coordination of the oropharyngeal swallow and is essential for normal function of mastication, formation, manipulation, and transportation of the bolus into the pharynx. (Wilson & Green, 2006) During the normal adult swallow, food is masticated, manipulated throughout the mouth and formed into a cohesive bolus with the tongue. (Wilson & Green, 2006) The bolus is then pressed superiorly against the hard palate with the anterior tongue and propelled posteriorly to the base of tongue and pharynx. The base of tongue and pharyngeal wall then approximate to propel the bolus into the esophagus and clear any pharyngeal residue. (Wilson & Green, 2006) Lingual propulsion requires significant coordination among the biomechanically coupled regions and is characterized by the sequential elevation of the anterior, middle, and dorsal regions of the tongue. (Wilson & Green, 2006)

When dysfunction arises in the lingual mechanism, it is targeted through rehabilitative strategies that target range of motion or strengthening. Range of motion exercises are designed to improve or maintain graded movements and flexibility of the jaw, tongue, and larynx. Tongue range of motion exercises may involve a combination of protrusion, lateralization, and/or posterior movements in a gargle-like posture. Lingual strengthening exercises are designed to improve the driving pressures of the tongue during the swallow, increase musculature, and improve bolus control and residue clearance. Exercises can be isometric, also called static strength training or endurance, or maximum isometric pressure, or unsustained maximum force. The oral tongue is targeted with tongue presses against a tongue depressor, inside of the cheek, or similar external aid for resistance. These presses can be practiced with protrusion, lateralization, elevation, and depression. Although the most effective intensity and dosage of exercises have not yet been determined, multiple repetitions of an exercise are prescribed, for multiple sessions per day, multiple days per week. (Pauloski, 2008)

Changes in tongue strength can be monitored in a variety of ways. Strength may be objectively measured with a device such as the Iowa Oral Pressure Instrument (IOPI) (an instrument designed for sustained superior tongue presses against the hard palate) or the SwallowSTRONG (a mouth piece with sensors also designed for superior tongue presses).(Sanfilippo & Lazarus, 2010) Recently studies have suggested that MRI may be useful to evaluate the swallowing mechanism, including the tongue, as it might provide new data for swallowing intervention or preoperative counseling of patients. (Tanaka et al., 2014) Patients treated for oropharyngeal cancers commonly undergo standard pretreatment MRI as part of their diagnostic work-ups, and the additional evaluation of structures is feasible. (Tanaka et al., 2014) Patient and clinician rated questionnaires are also sensitive to lingual strength changes, as lingual weakness my impact the person holistically, altering mealtimes and social experiences as previously described. Studies have correlated tongue strength with patient-related quality of life as rated with the EAT-10 and MDADI, and the domains of pain, swallowing, and speech on the European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Head and Neck module (QLQ-H&N35). (Belafsky et al., 2008)

2.6.1 Lingual Strengthening in Healthy and Disordered Populations

Lingual strengthening exercises have been found to be beneficial for a number of populations. A study conducted by Robbins and colleagues with healthy older adults, reported an 8-week progressive lingual resistance exercise program significantly increasing lingual isometric strength, thus increasing swallow pressures even though the study did not include a swallowing task. (2005) In addition to increased lingual pressure, Robbins and colleagues found increase in lingual volume and muscle mass as a pre-post treatment measure with MRI. (Robbins et al., 2005) A study by Lazarus and colleagues compared three groups of healthy normals. One treatment group receieved 'standard' tongue strengthening exercises with a tongue depressor, and the other treatment group received tongue strengthening exercises with the IOPI (providing patients with biofeedback). Both treatment groups made significant gains over the control group, but were not significantly different from each other, suggesting a tongue depressor, without biofeedback, was just as effective as the more expensive device with digital biofeedback. (Lazarus et al., 2003)

A study by Butler and colleagues on a population of healthy older adults revealed that participants who aspirated (38% of participants) had significantly less isometric tongue strength and swallowing tongue strength when compared to the non-aspirators. (2010) The study conducted by Robbins and colleagues demonstrated a decline in PAS scores after the 8-week treatment, supporting this theory. (2005) Authors noted that patients had reduced oropharyngeal residue after using the IOPI protocol in addition to the other benefits already described. (Robbins et al., 2005) This suggests that improving bolus control may prevent loss of bolus into the airway before the swallow and improving oropharyngeal clearance may prevent residue from entering the airway after the swallow. (Butler et al., 2010)

Lingual strengthening exercises were also implemented for patients who had neurological insults. Robbins and colleagues conducted a study with patients who had ischemic strokes, where again, only isometric exercises were given, without dynamic swallowing exercises. Increased pressure generation was noted in this population, as well. (Robbins et al., 2007) In line with the study by Robbins and colleagues, Juan and colleagues published visible lingual changes on MRI in a case study of a patient who had a stroke.

Authors reported an 8.37% increase in lingual volume when intrinsic and extrinsic tongue muscles after 8 weeks of therapy. (Juan et al., 2013)

2.6.2 Lingual Strengthening in the HNC Population

Lingual strengthening exercises are not always included in protocols for patients with HNC, limiting the available studies that investigate their use. A large percentage of available studies treat the patients reactively, post-surgical intervention or C/RT. In a case study conducted by Sullivan and colleagues, the effects of tongue strengthening exercises were investigated in a surgically treated oral cancer patient. (Sullivan et al., 2001) This study found that tongue strength and swallow function improved with the exercises programs; the patient was also able to upgrade his diet. (Sullivan et al., 2001) Prasse and colleagues conducted a study to determine the effect of two types of exercise programs on tongue function and swallowing in patients with oral cancer treated with CRT. (Prasse et al., 2009) Tongue strength was not statistically different following the exercise program in either group; tongue strength also did not differ between the groups. (Prasse et al., 2009) However, a significant improvement of quality of life was noted in the experimental arm. (Prasse et al., 2009) A study by Lazarus and colleagues examined the effects of an isometric tongue strengthening program in comparison to traditional therapy on tongue strength, oropharyngeal swallow function, and QOL for patients with oral and oropharyngeal cancer treated with C/RT. (Lazarus et al., 2014) Tongue strengthening did not yield a statistically significant improvement in either tongue strength or swallowing measures in this study. However, QOL in the eating and speech domains improved following treatment. (Lazarus et al., 2014) Participant adherence was relatively poor in this study and was slightly worse in the treatment arm. Further, his study only included lingual ROM, strengthening, and one laryngeal ROM exercise, and suggested other types of exercises (I.e. pharyngeal strengthening) may need to be included too. (Lazarus et al., 2014)

Within the few published studies that include lingual exercises in a prophylactic protocol, concomitantly prescribed lingual range of motion exercises are common. These exercises require the tongue to move in similar directions as the strengthening exercises (protrusion, lateral, etc.) but do not require the participant to press with force against resistance. A study by Peng and colleagues suggested participants in the treatment arm maintained function post-treatment while participants in the treatment arm presented with a worsened swallowing condition as indicated by the Functional Outcome Swallowing Scale (FOSS). (Peng et al., 2015) Further, participants who were nonadherent in this study were also identified as having a significantly worse FOSS than adherent participants. (Peng et al., 2015) Duarte and colleagues conducted a study with similar findings. (2013) The authors also prescribed a protocol including lingual range of motion and strengthening exercises. (Duarte et al., 2013) Results suggested a significant difference with diet change, with more of the adherent patients maintaining or improving their diet from pretreatment to one-month post-treatment in comparison to those who were nonadherent with exercises. (Sullivan, 2001)

In summary, tongue function is commonly impacted through presence of tumor and acute and late effects of CRT. Research in healthy and disordered populations has suggested positive benefit for swallow function and tongue strength when exercises specific to tongue strength are included in the protocol. For the head and neck cancer population, benefit may be recognized solely as maintenance of function. In the current evidence, it is suggested that adherent participants have superior outcomes than those who are nonadherent. It is unclear which variable is the cause of benefit in these studies: the timing of intervention, the inclusion of a lingual strengthening exercise, the addition of a lingual range of motion exercise to further manipulate the mechanism, other exercises prescribed within the protocol, or simply the act of maintaining maximum possible activity of the swallow mechanism (whether that is by adhering to swallow protocols or following a PO (by mouth) diet).

2.7 Summary

Dysphagia presents in the HNC population as a consequence of the tumor altering bolus flow and anatomical motility or the damaging effects of oncologic treatment. (Lazarus, 2006) Post radiation swallow function may be impaired due to a number of reasons including neuropathy, edema, fibrosis, and atrophy. (61) Lingual strength can be impacted through atrophy consequence of disuse during radiotherapy or hypoglossal palsy. (Learned et al., 2012) Lingual strength and motility may be further compromised with late-effect fibrotic changes. (Strojan et al., 2017) Prophylactic swallowing exercises have been widely recommended to maintain function of the swallowing mechanism; however, evidentiary support is limited due to lack of standardized protocol and measures. (Greco et al., 2018) The literature currently supports the role of lingual strengthening exercises as a part of prophylactic intervention for patients with head and neck cancer experiencing oropharyngeal dysphagia.

CHAPTER 3. METHODS

3.1 Eligibility Criteria

Studies were eligible for inclusion where they met the following PICO criteria. Participants were adults diagnosed with HNC and treated with radiation therapy or chemo-radiotherapy. Interventions that were eligible included programs designed to prevent/reduce dysphagia from occurring and have lasted more than one session. Behavioral intervention must have been provided by a speech-language pathologist or other trained healthcare professionals and include a lingual strengthening component, specific to the oral tongue (tongue press, etc.). Exercises must have been introduced and initiated prior to radiation or chemo-radiotherapy. Studies that included a comparator group were eligible for inclusion. The comparator could have received no treatment (non-active comparator), usual care (active or non-active) or a different treatment (active) or sham exercise (active). At least one swallow-related outcome measure (physiologic changes, functional changes, or swallow-related quality of life) must have been reported. Data could be extracted from patient reports or questionnaires, clinician rated measures, or instrumental swallowing evaluations. Studies were excluded if participants had a history of surgical intervention or if lingual range of motion exercises were also included in the study.

3.2 Identification of Studies

Four electronic health databases were searched: Medline, PubMed, CINAHL, and the Cochrane Library. Additional searches were conducted with Google Scholar and through reference lists of directly relevant articles and systematic reviews. The search strategy was developed and followed by speech language pathologist (D.S) and graduate student (C.P.). C.P. and D.S., masked, identified studies for inclusion from the searched collection of abstracts and full-text and evaluated each study for methodologic rigor. Results/data of each article were masked to the authors during the selection period. One author (C.P) extracted data from the articles for analysis and results were confirmed by (D.S). Authors were contacted, when necessary, to provide missing information and confirm completion dates of proposed research. All disagreements were resolved by consensus.

The search was limited to peer reviewed studies, published in English, that were conducted with human subjects. No restrictions were placed on date of publication; all dates through November 2018 were included. All study types and levels of evidence were included in this search.

The search was completed on November 4, 2018. Search terms are defined for study selection process in Table 3.1. Three studies met criteria for review. The study selection process is outlined in the PRISMA diagram (Figure 3.1). Authors agreed upon selected studies.

Table 3.1 Overview of Study Selection Process

Database	# Articles Found	# Reviewed	Search Terms
Medline (EBSCOHOST) Oct. 10, 2018	7	4	Exercise AND swallowing AND head and neck cancer Advanced search: human, English language, apply related words, full text linked, apply equivalent subjects
CINAHL Oct. 9, 2018	197	37	Exercise AND swallowing AND head and neck cancer Advanced search: apply related words, human, search within full text, apply equivalent subjects, full text, English, peer-reviewed
Cochrane Library Oct. 9, 2018	70 (10 Cochrane reviews, 2 Cochrane protocols, 58 trials)	29	Exercise AND swallowing AND head and neck cancer [all text] Advanced search: all dates, all years, search word variations
PubMed Oct. 24, 2018	33		(("exercise"[MeSH Terms] OR "exercise"[All Fields] OR "exercises"[All Fields] OR "exercise therapy"[MeSH Terms] OR ("exercise"[All Fields] AND "therapy"[All Fields]) OR "exercise therapy"[All Fields]) AND ("deglutition"[MeSH Terms] OR "deglutition"[All Fields] OR "swallowing"[All Fields])) AND ("head and neck neoplasms"[MeSH Terms] OR ("head"[All Fields] AND "neck"[All Fields] AND "neoplasms"[All Fields]) OR "head and neck neoplasms"[All Fields] OR ("head"[All Fields] AND "neck"[All Fields] AND "cancer"[All Fields]) OR "head and neck cancer"[All Fields])
Other Means Nov. 4, 2018	44	36	Obtained through Google Scholar, and reference lists of articles located in the current search
Totals:	351	106	
	Final selection:	3	

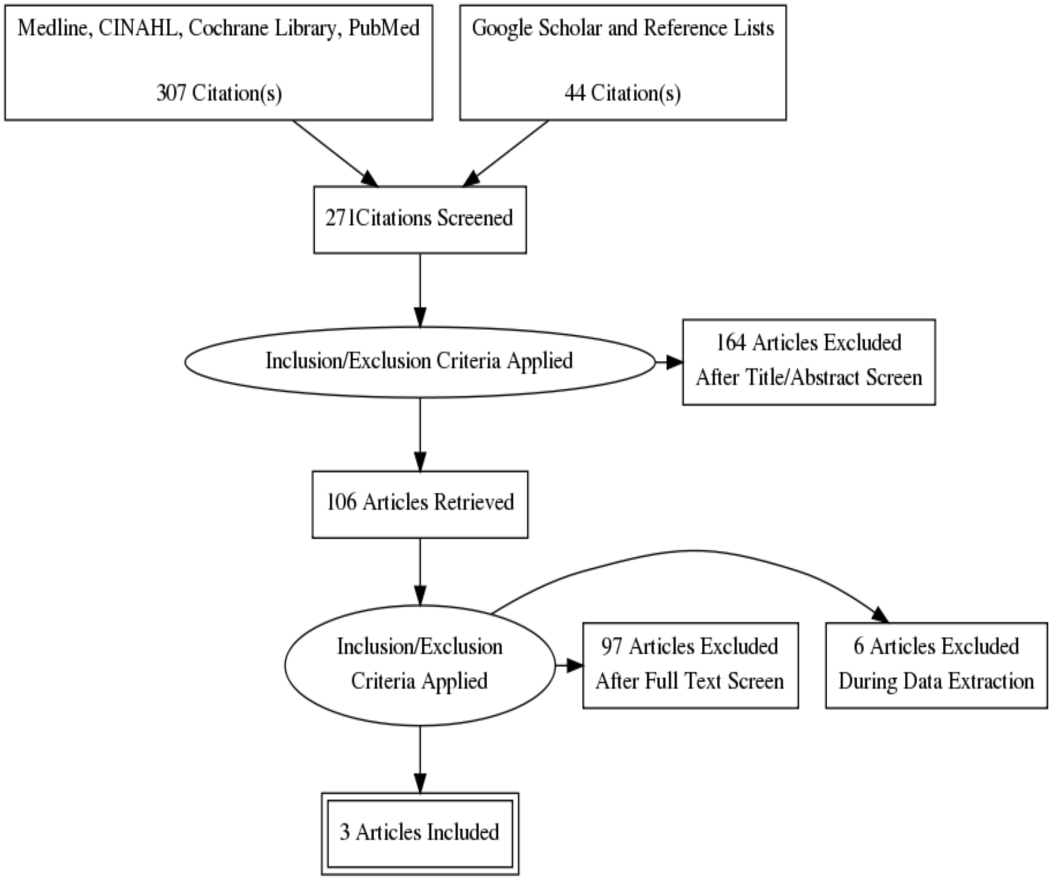

Figure 3.1 PRISMA Diagram

3.3 Study Quality

For consistency with other reviews, data were extracted on study quality using an 12-item checklist, described by Furlan and colleagues. (Furlan et al., 2009) This checklist has been used previously to assess the quality of dysphagia clinical trials. (Furlan et al., 2009) Each of the 12 items is given a score of 1 if the criterion is met, yielding a summary score of 0 (lowest) to 12 (highest quality). Scores of ≥6 reflect studies with a "low risk of bias, while scores lower than six represent a "high risk of bias". (Furlan et al., 2009) Internal validity criteria refer to characteristics of the study that might be related to selection bias (criteria 1, 2, 9), performance bias (criteria 3, 4, 10, 11), attrition bias (criteria 6, 7), and detection bias (criteria 5, 12). Criteria for judgement of bias and sources of bias are outlined in Figures 3.2 and 3.3. Studies were not excluded on the basis of quality because we aimed to ascertain any evidence, however weak, of potential effects of lingual strengthening exercises on outcome measures. The checklist was trialed on related articles, not included within the review to ensure common interpretation of the items and their operationalization. Authors then independently analyzed the studies included within the review. Any disagreements were resolved by consensus.

1	A random (unpredictable) assignment sequence. Examples of adequate methods are coin toss (for studies with 2 groups), rolling a dice (for studies with 2 or more groups), drawing of balls of different colors, drawing of ballots with the study group labels from a dark bag, computer-generated random sequence, pre-ordered sealed envelops, sequentially-ordered vials, telephone call to a central office, and pre-ordered list of treatment assignments Examples of inadequate methods are: alternation, birth date, social insurance/security number, date in which they are invited to participate in the study, and hospital registration number.
2	Assignment generated by an independent person not responsible for determining the eligibility of the patients. This person has no information about the persons included in the trial and has no influence on the assignment sequence or on the decision about eligibility of the patient.
3	This item should be scored "yes" if the index and control groups are indistinguishable for the patients or if the success of blinding was tested among the patients and it was successful.
4	This item should be scored "yes" if the index and control groups are indistinguishable for the care providers or if the success of blinding was tested among the care providers and it was successful.
5	Adequacy of blinding should be assessed for the primary outcomes. This item should be scored "yes" if the success of blinding was tested among the outcome assessors and it was successful or: –for patient-reported outcomes in which the patient is the outcome assessor (*e.g.*, pain, disability): the blinding procedure is adequate for outcome assessors if participant blinding is scored "yes" –for outcome criteria assessed during scheduled visit and that supposes a contact between participants and outcome assessors (*e.g.*, clinical examination): the blinding procedure is adequate if patients are blinded, and the treatment or adverse effects of the treatment cannot be noticed during clinical examination –for outcome criteria that do not suppose a contact with participants (*e.g.*, radiography, magnetic resonance imaging): the blinding procedure is adequate if the treatment or adverse effects of the treatment cannot be noticed when assessing the main outcome –for outcome criteria that are clinical or therapeutic events that will be determined by the interaction between patients and care providers (*e.g.*, co-interventions, hospitalization length, treatment failure), in which the care provider is the outcome assessor: the blinding procedure is adequate for outcome assessors if item "4" (caregivers) is scored "yes" –for outcome criteria that are assessed from data of the medical forms: the blinding procedure is adequate if the treatment or adverse effects of the treatment cannot be noticed on the extracted data
6	The number of participants who were included in the study but did not complete the observation period or were not included in the analysis must be described and reasons given. If the percentage of withdrawals and drop-outs does not exceed 20% for short-term follow-up and 30% for long-term follow-up and does not lead to substantial bias a "yes" is scored. (N.B. these percentages are arbitrary, not supported by literature).
7	All randomized patients are reported/analyzed in the group they were allocated to by randomization for the most important moments of effect measurement (minus missing values) irrespective of non-compliance and co-interventions.
8	In order to receive a "yes", the review author determines if all the results from all pre-specified outcomes have been adequately reported in the published report of the trial. This information is either obtained by comparing the protocol and the report, or in the absence of the protocol, assessing that the published report includes enough information to make this judgment.
9	In order to receive a "yes", groups have to be similar at baseline regarding demographic factors, duration and severity of complaints, percentage of patients with neurological symptoms, and value of main outcome measure(s).
10	This item should be scored "yes" if there were no co-interventions or they were similar between the index and control groups.
11	The reviewer determines if the compliance with the interventions is acceptable, based on the reported intensity, duration, number and frequency of sessions for both the index intervention and control intervention(s). For example, physiotherapy treatment is usually administered over several sessions; therefore it is necessary to assess how many sessions each patient attended. For single-session interventions (e.g., surgery), this item is irrelevant.
12	Timing of outcome assessment should be identical for all intervention groups and for all important outcome assessments.

Figure 3.2 Criteria for a Judgement of "Yes" for the Sources of Risk of Bias

A	1. Was the method of randomization adequate?	Yes/No/Unsure
B	2. Was the treatment allocation concealed?	Yes/No/Unsure
C	Was knowledge of the allocated interventions adequately prevented during the study?	
	3. Was the patient blinded to the intervention?	Yes/No/Unsure
	4. Was the care provider blinded to the intervention?	Yes/No/Unsure
	5. Was the outcome assessor blinded to the intervention?	Yes/No/Unsure
D	Were incomplete outcome data adequately addressed?	
	6. Was the drop-out rate described and acceptable?	Yes/No/Unsure
	7. Were all randomized participants analysed in the group to which they were allocated?	Yes/No/Unsure
E	8. Are reports of the study free of suggestion of selective outcome reporting?	Yes/No/Unsure
F	Other sources of potential bias:	
	9. Were the groups similar at baseline regarding the most important prognostic indicators?	Yes/No/Unsure
	10. Were co-interventions avoided or similar?	Yes/No/Unsure
	11. Was the compliance acceptable in all groups?	Yes/No/Unsure
	12. Was the timing of the outcome assessment similar in all groups?	Yes/No/Unsure

Figure 3.3 Sources of Risk of Bias

3.4 Data Extraction

Data were extracted in the following areas: study characteristics (author, year, country of origin, setting, type of study), patient characteristics (cancer site, oncologic treatment, intervention group, sample size, age range, gender), intervention (type and dosage of intervention and comparator groups), and outcome measures (all swallow related outcomes and timing of follow-up). It was anticipated that the studies included in this review would present with heterogeneous interventions, types of outcome measures, and timing of data points. Interventions were divided into five categories: jaw range of motion; lingual range of motion and strengthening; laryngeal range of motion; and pharyngeal strengthening. Outcome data were divided into three categories: physiologic (changes in the anatomy or function of the swallow mechanism as indicated by MRI, VFSS, etc), quality of life impact (self-reported or clinician-rated questionaires, etc), and functional outcomes (means of nutrition, weight loss, diet, taste, smell, etc). For this review, the authors were interested in significant change present in outcome measures sensitive to the effects of lingual strengthening intervention.

One author (C.P) extracted data for all included studies. A speech-language pathologist (D.S) independently extracted data for one randomly selected study to ensure reliability.

3.5 Analysis

A meta-analysis was not appropriate for use in this review due to the small number of studies and variation among interventions and outcome measures. Further, outcome measures were obtained at various follow-up times. A qualitative method of analysis was selected to summarize significant findings and relationships among the data.

CHAPTER 4. RESULTS

4.1 Study Selection

The search identified 351 articles., 106 articles were reviewed after title and abstract screenings. Nine articles met inclusion/exclusion criteria. Six additional articles were excluded prior to data extraction due to presence of lingual range of motion exercises and/or patient history of surgical intervention. Three studies were selected as eligible for review.

4.2 Study Characteristics

All studies were completed within the last fifteen years, 2012 (Carnaby-Mann et al.), 2008 (Carroll et al.), and 2006 (Kulbersh et al.) at university hospitals within the United States. One randomized control trial with parallel groups (Carnaby-Mann et al., 2012), one prospective cohort study with cross-sectional quality of life analysis (Kulbersh et al., 2006), and one retrospective case control study (Carroll et al., 2008) were included within this systematic review.

4.3 Quality Assessment

Quality assessment scores are described in Table 4.1. One study achieved a score greater than or equal to six (Carnaby-Mann et al., 2012), classifying the study as having a "low risk of bias". Two studies (Kulbersh et al., 2006; Carroll et al., 2008) had scores of 0 and 4 respectively, indicating "high risk of bias".

Table 4.1 Risk of Bias

	(Carnaby-Mann et al., 2012)	(Kulbersh et al., 2006)	(Caroll et al., 2008)
A. Randomization adequate	+	n/a	n/a
B. Allocation concealed	+	n/a	n/a
C. Patient blind	-	-	-
Care provider blind	-	-	-
Assessor blind	+	-	+
D. Acceptable withdrawal rate	-	?	+
Patients analyzed in respective groups	+	+	-
Free of selective outcome reporting	?	?	?
E. Similar groups at baseline	+	-	+
F. Co-intervention controlled	+	-	?
Acceptable compliance	-	?	?
Timing of outcome	+	-	+
Total	7	1	3

4.4 Patient Characteristics

Table 4.2 highlights the characteristics of the 113 patients included. Primary sites were as follows: base of tongue 24 (21%), tonsil 25 (22%), pharyngeal wall 5 (4%), unspecified oropharynx 17 (15%), unspecified larynx 8 (7%), unspecified nasopharynx 1 (.8%), unspecified hypopharynx 1 (.8%), unspecified neck 1 (.8%), and unspecified sites of the head and neck 31 (27%). Reported oncologic treatments are summarized in Table 4.2 and included participants treated with external beam radiation and others with combined chemo-radiotherapy. Mean ages of intervention groups ranged from 54 to 60.7

years. Seventy four percent of subjects were males (n=84) and twenty-six percent were females (n=29). Fifty-four patients were assigned to treatment groups that received prophylactic intervention with a lingual strengthening component, a total of forty-four males and ten females.

Table 4.2 Patient Characteristics

	(Carnaby-Mann et al., 2012)		(Kulbersh et al., 2006)		(Carroll et al., 2006)	
Sample size	**Total:** 58 **Intervention A (usual care):** 20 **Intervention B (standardized sham):** 18 **Intervention C (Pharyngocise):** 20		**Total:** 37 **Pretreatment Group:** 25 **Posttreatment Group:** 12		**Total:** 18 **Pretreatment group**: 9 **Posttreatment group**: 9	
Mean age	**Intervention A:** 54 +/- 11.3 **Intervention B:** 60 +/- 12.2 **Intervention C:** 59 +/- 10.4		**Pretreatment Group:** 55.1 +/- 9.6 **Posttreatment Group:** 60.3 +/- 10		**Pretreatment group:** 57.5 **Posttreatment group:** 60.7	
Gender	**Intervention A:** 15 males ; 5 females **Intervention B:** 11 males ; 7 females **Intervention C:** 18 males ; 2 females		**Pretreatment Group:** 19 males ; 6 females **Posttreatment Group:** 9 males ; 3 females		**Pretreatment group:** 7 males ; 2 females **Posttreatment group:** 5 males ; 4 females	
Tumor Site	**Intervention A:** (mode)		**Pretreatment Group:**		**Pretreatment Group:**	
			Base of tongue	12	Oropharyngeal	
	Base of tongue	3	Tonsil	7	Oropharyngeal	7
			Oropharynx	2	Hypopharynx	
	Tonsil	9	Pharyngeal Wall	2	Larynx	2
			Supraglottis/Larynx	2	Oropharyngeal	
	Intervention B: (mode)		Nasopharynx	0	Hypopharyngeal	0
			Neck	0	Hypopharynx 1	

Table 4.2 Patient Characteristics Continued

	Base of tongue	3	**Posttreatment Group:**		**Posttreatment Group:**	
			Base of tongue	1		
	Tonsil	4	Tonsil	2	Oropharyngeal	7
			Oropharynx	1		
	Intervention C: (mode)		Pharyngeal Wall	3	Larynx	1
			Supraglottis/Larynx	3		
	Base of tongue	5	Nasopharynx	1	Hypopharyngeal	1
			Neck	1		
	Tonsil	3				
Oncology Treatment	**Intervention A:**		Unspecified radiation or combined chemoradiation treatment.		All participants received chemoradiation treatment.	
	Conventional radiotherapy	9				
	IMRT	11				
	Plus chemotherapy	10				
	Intervention B:					
	Conventional radiotherapy	6				
	IMRT	12				
	Plus chemotherapy	6				
	Intervention C:					
	Conventional radiotherapy	9				
	IMRT	11				
	Plus chemotherapy	6				

4.5 Intervention Characteristics

Carnaby Mann and colleagues established three treatment groups: usual care, standardized sham treatment, and high intensity behavioral treatment ("pharyngocise"). In the usual care (control) group, if treatment was offered, it included supervision of feeding and education of safe swallowing precautions (positioning and slowed rates of feeding) by the hospital speech pathology service. These patients participated in telephone calls with a research assistant on a weekly basis to monitor swallowing outcomes. The standardized sham group was given a buccal extension maneuver ("valchuff") exercise and appropriate diet modification (under direction of SLP) twice daily for the duration of CRT. Patients were instructed to complete the exercise for 10 repetitions over four cycles, each of 10 minutes duration. The pharyngocise group was given a battery of exercises: falsetto, tongue press, hard swallow, jaw resistance/strengthening using the Therabite Jaw Motion Rehabilitation System, and diet modification (under direction of SLP) twice daily for the duration of CRT. Patients in this group were instructed to complete the four exercises for 10repetitions over four cycles, each of 10 minutes duration. These 40-45 minute sessions were to be completed twice per day. The tongue press exercise was not thoroughly described in this article. After contacting the author, it was determined that the participants utilized tongue depressors. However, during RT, at approximately 4 weeks into treatment, patients were no longer able to tolerate the tongue depressors due to mucositis and pain. At that time, the tongue exercises were modified with the patient pressing their tongue to the palate. SLPs monitored their efforts by feeling beneath their chin . (Carnaby-Mann, Personal Communication, March 25, 2019)

Kulbersh and colleagues and Carroll and colleagues both utilized a variation of the UAB protocol for the participants of treatment groups in their studies. Exercises included Masako, tongue resistance (five second holds for each of four positions), Mendelsohn maneuver (five second holds), and Shaker exercises. Kulbersh and colleagues also utilized the falsetto exercise, while Carroll and colleagues chose to include the effortful swallow. Dosages for both studies were the same. The isometric Shaker exercise was held for one minute, followed by one minute of rest. The isotonic Shaker exercise was completed with 30 repetitions. Other exercises were assigned at 10 repetitions, five times per day. The tongue resistance exercise was described as isometric. The patients firmly pressed against a tongue depressor or spoon in an upward motion toward the palate, left, right, and forward toward the front teeth.

Kulbersh and colleagues allocated patients into two groups in their study: a pretreatment and posttreatment group. The pretreatment group initiated swallowing exercises two weeks prior to CRT and returned to the clinic at the second and sixth week of their radiation treatment to monitor compliance and progress. The posttreatment group initiated exercises at the first visit after the initiation of their treatment. This group also returned at the second and sixth week. Both groups were provided with the previously described, modified UAB dysphagia protocol. Carroll and colleagues defined two groups in their study: a pretreatment group and a post-treatment group. The pretreatment group initiated swallowing exercises two weeks prior to CRT. The swallowing intervention provided to the post-treatment group was briefly described as "standard practice... received posttreatment as swallowing problems arose". All patients had PEG tubes prophylactically placed prior to CRT.

Carnaby-Mann and colleagues included exercises from four categories: jaw and laryngeal range of motion, and pharyngeal and lingual strengthening. Kulbersh and Carroll and colleagues both utilized variations of the UAB protocol which includes exercises that target laryngeal range of motion, and pharyngeal and lingual strength. Interventions are summarized and categorized for the treatment group in Table 4.3.

Table 4.3 Intervention Characteristics

	Description of Intervention	Types of Intervention in Treatment Group				
		ROM jaw	ROM laryngeal	ROM lingual	Strength Pharynge-al	Strength lingual
(Carnaby-Mann et al., 2012)	***Intervention A:*** (if offered) supervision for feeding and precautions for safe swallowing (e.g. positioning, slowed rate of feeding) by the hospital SLP ***Intervention B:*** dietary modification by study SLP. Exercises: buccal extension maneuver ("Valchuff ") exercise X 10 repetitions = 1 cycle 1 cycle = ~10 minutes 4 cycles = one ~ 45 minute session ***Intervention C:*** dietary modification by study SLP Exercises: falsetto, tongue press, hard swallow, and jaw resistence (using the Therabite Jaw Motion Rehabilitation System) Each exercise X 10 repetitions = 1 cycle 1 cycle = ~10 minutes 4 cycles = one ~45 minute session	+ Thera-bite	+ Falsetto	-	+ Hard swallow	+ Tongue press
(Kulbersh et al., 2006)	**All participants were trained for a variation UAB Swallowing Protocol** <u>*Laryngeal/phayngeal exercises:*</u> Fasetto(10 repetitions = 1 set, 5 sets per day), Masako (10 repetitions = 1 set, 5 sets per day), isometric Shaker(1 min hold/rest, 3 repetitions per set, 5 sets per day); isotonic Shaker (30 repetitions per set, 5 sets per day) and Mendelsohn (holding the larynx in an elevated position for 5 seconds, 10 repetitions = 1 set, 5 sets per day) <u>*Lingual exercises:*</u>	-	+ Shaker, Mendelsohn, Falsetto	-	+ Masako	+ Tongue press

Table 4.3 Intervention Characteristics Continued

	tongue press against depressor or spoon side, and forward toward the front teeth (10 repetitions each per set, with 5 second holds; 5 sets per day) The posttreatment group did not initiate exercises until the conclusion of RT or CRT.					
(Carroll et al., 2008)	**Treatment group participants were trained for a variation of UAB Swallowing Protocol** *Laryngeal/phayngeal exercises:* effortful swallow (10 repetitions = 1 set, 5 sets per day), Masako (10 repetitions = 1 set, 5 sets per day), isometric Shaker(1 min hold/rest, 3 repetitions per set, 5 sets per day); isotonic Shaker (30 repetitions per set, 5 sets per day) and Mendelsohn (holding the larynx in an elevated position for 5 seconds, 10 repetitions = 1 set, 5 sets per day) *Lingual exercises:* tongue press against depressor or spoon upward toward the palate, right and left side, and forward toward the front teeth (10 repetitions each per set, with 5 second holds; 5 sets per day) **Control Group:** post treatment management as needed; duration: unknown	-	+ Shaker, Mendelsohn	-	+ Effortful swallow Masako	+ Tongue press

4.6 Outcome Characteristics

Results were analyzed on different timelines with each study. Only one study (CM) collected data before the initiation of cancer treatment as well as post-intervention data; the other two studies collected post-intervention data only. Carnaby-Mann and colleagues (2012) collected data before initiation of CRT, at competition of CRT, and 6 months post-completion of CRT. Kulbersh and colleagues (2006) collected pre-treatment group data 6 to 12 months post-CRT with a median of nine months. For the post-treatment group, Kulbersh and colleagues collected data between 6 and 20 twenty months with a median of fourteen months. Carroll and colleagues' (2008) study obtained physiological outcomes at approximately 3 months post-CRT and functional outcomes 1 year post-CRT.

Carnaby-Mann and colleagues (2012) documented the following measures: change in muscle size and composition (with T2-weighted MRI), Functional Oral Intake Scale Score (FOIS), Mann Assessment of Swallowing Ability (MASA) scores confirmed with videoendoscopic and videofluroscopic evaluation, mouth opening, nutritional status (measured by weight), dysphagia-related complications (e.g. pneumonia, dehydration), unstimulated saliva production (measured by standard saliometric techniques), smell and taste perception (measured by University of Pennsylvania Smell Identification Test). The FOIS is a 7 point scale that reflects patient's level of intake rather than a direct reflection of the existing impairment or anatomical/physical deficits. It ranges from a 1, which indicates 100% impairment, no oral intake, and complete tube dependence, to a 7, which indicates total oral intake with no restrictions. (Crary, Mann, & Groher, 2005) The MASA is a standardized clinical swallow evaluation that rates the following components on a scale of 1-5 or 1-10: alertness, cooperation, auditory comprehension, respiration, respiratory rate, dysphagia, dyspraxia, dysarthria, saliva, lip seal, tongue movement, tongue strength, tongue coordination, oral preparation, gag, palate, oral transit, cough reflex, voluntary cough, voice, trach, pharyngeal phase, pharyngeal response, and diet and fluid recommendations. Lower total numbers are correlated with increased severity of dysphagia. (Carnaby-Mann & Lenius, 2008)

Kulbersh and colleagues (2006) documented outcomes through use of the M.D. Anderson Dysphagia Inventory (MDADI). MDADI is a 20-item self-administered questionnaire that quantifies swallowing-related quality of life. The MDADI quantifies an individual's global (G), physical (P), emotional (E), and functional status in attempts to create a holistic picture of the patient. Summary and subscale MDADI scores are normalized to range from 20 (extremely low functioning) to 100 (high functioning). (Hutcheson et al., 2016) These scores were reported as unadjusted and adjusted after controlling for age, race, stage, site of tumor, follow-up time, and type of treatment. Although no questions on the survey directly target perception of tongue function, it could be a factor in an "agree" response to the statement "it takes me longer to eat".

Carroll and colleagues (2008) obtained a VFSS examination at three months post-treatment for all enlisted participants, in lateral and anteroposterior positions. Recorded examinations were used to evaluate hyoid elevation, tongue base position and movement, epiglottis inversion, cricopharyngeal opening, and Penetration Aspiration Score. Presence/use of a PEG tube was documented at 12 months post-treatment. Epiglottis inversion was measured on a three-point scale of normal inversion, impaired inversion, or no inversion. All other measurements were measured as a difference in movement from a reference point.

4.7 Significant Findings

In attempts to compare a variety of outcome measures across studies, outcomes were grouped as physiologic (anatomical or physiologic signs determined through objective measures or instrumental evaluations), quality of life (patient or clinician completed questionnaires concerning impact of dysphagia on daily life), and functional (current diet, alternative means of nutrition, or related symptoms of swallow dysfunction). Outcomes hypothesized as sensitive to lingual strengthening include the T-2 weighted MRI (with measurements specific to the length, width, and T2 relaxation time of the genioglossus muscle and and T2 relaxation time of the hyoglossus muscle), and the FOIS, MASA, diet consistency, and the compiled functional swallowing outcome.. The MDADI scores reported by Kulbersh and colleagues may also be sensitive to lingual strengthening exercises. In the study conducted by Carrol and colleagues, outcome measures sensitive to lingual strengthening exercise could be the Penetration Aspiration Scale in conjunction with observations made during the VFSS and impact PEG tube presence.

4.8 Physiologic Outcomes

As determined by T2 MRI, muscle size demonstrated greater preservation and T2 relaxation times were significantly reduced in the pharyngocise group. More specifically, the genioglossus, mylohyoid, and hyoglossus muscles showed more deterioration in the usual care group, than in the Pharyngocise group. (Carnaby-Mann et al., 2012) There was less reduction in MASA scores for the treatment group, in comparison to the control group, from baseline to immediate-post CRT. The MASA includes assessment components such as tongue strength, oral preparation, and oral transit times. However, these components were not reported on. The pharyngocise group also demonstrated greater median FOIS scores, although not significant.

4.9 Quality of Life Outcomes

Kulbersh and colleagues (2006) reported significant difference between the participant groups for swallowing QOL in three of four domains (global, emotional, physical, and overall MDADI score). The adjusted means showed even a greater difference between the two groups for each of the four domains of the MDADI (global, emotional, functional, and physical) when compared to the unadjusted data. The patients performing pre-treatment swallowing exercises scored significantly higher than patients performing post-treatment swallowing exercises on the global assessment score and the physical and emotional subscales. Significant results suggest positive effect of pretreatment exercises on swallow-related QOL, affective response to the swallowing disorder, and self-perceptions of their swallowing difficulty.

4.10 Functional Outcomes

Functional swallowing ability deteriorated less in the Pharyngocise group than in the usual care or sham groups. Functional swallowing compiled the following data: weight loss less than 10%, maintenance of oral diet, and a change of less than 10 points on the Mann Assessment of Swallowing Ability. Pharyngocise participants maintained oral feeding more often than those in the usual care group (42% vs. 14% respectively), and fewer subjects received gastronomy tube feedings. Patients in treatment groups were also more readily able to return to their pre-CRT diet without swallow-related complications. Carnaby-Mann and colleagues (2012) calculated that a patient receiving Pharyngocise treatment has a six-time greater chance for a favorable outcome than a patient who did not receive preventative exercises during CRT.

4.11 Summary of Findings

The studies in this review included a variety of rehabilitation strategies in conjunction with lingual strengthening exercises. These protocols were designed to improve oral and pharyngeal phase swallow functioning. Across studies, no two assessment measures were alike, and the timeline of outcome measures varied greatly, with only one study establishing baseline functioning pre-CRT. Significant results of these studies suggest greater preservation of lingual and submental muscle mass, an improvement in quality of life, maintenance of oral diet, less use of gastrostomy tube feedings, and ability to return to pre-CRT diet without swallow-related complications. Unfortunately, oropharyngeal swallow function did not demonstrably improve in these studies. Further, no study directly measured change in lingual strength; an objective effect of the exercises is unable to be established. As such, we were unable to find compelling evidence for inclusion of lingual strengthening exercises as part of a prophylactic swallow protocol.

Outcome measurements varied for each study and are outlined with reported results in Tables 4.6-4.8 and Figure 4.1.

Table 4.6 Summary of Findings (Carnaby-Mann et al., 2012)

(Carnaby-Mann et al., 2012)					
Identified Physiologic Changes		**Intervention A:** **(n=14)**	**Intervention B:** **(n=13)**	**Intervention C:** **(n=14)**	**P value:**
	T2 MRI	See Figure 4.1.			
	VFE				
	Baseline	0.186 +/- 0.09	0.272 +/- 0.15	0.214 +/-0.02	ns
	6 week outcome	0.214 +/- 0.09	0.343 +/-0.16	0.200 +/-0.16	
	Mouth opening				
	baseline	36.6 +/- 8.05	39.2 +/- 6.4	41.6 +/- 8.4	
	6 week outcome	32.3 +/- 5.9	34.07 +/- 7.3	40.05 +/-8.3	.047*
Quality of Life Outcomes	*MASA*				
	baseline	195.5 +/- 4	194.7 +/- 3.5	195.1 +/- 5.9	*ns*
	6 week outcome	171.5 +/- 14.2	173.6 +/- 11.8	177.14 +/- 12.5	.006*
	FOIS				
	baseline	*7*	*7*	*7*	*ns*
	6 week outcome	*4*	*4*	*5*	
Quality of Life Outcomes	*n/a*				
Functional Outcomes **(at 6 weeks)**	Normal diet	2	2	5	.185
	Nonoral feeding	6	3	3	.295
	Functional swallowing	2	2	6	.067*
	Weight loss (>10%)	6	6	4	.604
	Salivation loss	12	12	8	.061*
	Taste decline	10	13	9	.053*
	Smell decline	6	4	2	.123
	Any complication	7	4	5	.597*

Muscle	Study arm: Usual care	Sham	Pharyngocise	*p*
Genioglossus*				
Length				<.03
Before	37.08 ± 6.4	34 ± 4.7	34.9 ± 4.8	
After	33.6 ± 5.7	32.5 ± 3.9	34.4 ± 2.7	
Change	3.67	1.5	0.5	
Thickness				NS
Before	7.31 ± 1.9	7.41 ± 0.7	7.54 ± 1.8	
After	6.89 ± 0.7	6.97 ± 0.6	7.11 ± 1.8	
Change	0.42	0.43	0.44	
T_2				<.01
Before	108.1 ± 5.2	107 ± 6.6	111.2 ± 3.8	
After	108.05 ± 2.1	104.9 ± 4.1	101.6 ± 5	
Change	0.05	2.1	9.6	
Hyoglossus*				
Length				<.018
Before	21.04 ± 4.1	17.9 ± 4.1	17.4 ± 3.9	
After	17.2 ± 3.6	16.9 ± 3.4	17.9 ± 3.07	
Change	3.84	1	−0.05	
Thickness				NS
Before	4.11 ± 0.88	3.1 ± 0.73	2.9 ± 0.95	
After	3.06 ± 0.86	3.2 ± 0.9	2.5 ± 0.6	
Change	1.05	−0.1	0.4	
T_2				<.037
Before	104.2 ± 4.1	106.8 ± 6.2	114.7 ± 8.8	
After	104.9 ± 3.7	105.1 ± 2.6	105.1 ± 2.6	
Change	−0.07	1.7	9.6	
Mylohyoid*				
Thickness				<.021
Before	4.4 ± 1.1	2.86 ± 0.7	3.86 ± 0.96	
After	2.8 ± 0.78	3.01 ± 1.0	3.8 ± 1.2	
Change	1.6	−0.15	0.06	
T_2				<.017
Before	104.1 ± 4.6	103.7 ± 4.4	111.8 ± 11.3	
After	106.3 ± 6.5	104.1 ± 5.6	103.8 ± 3.4	
Change	−2.2	−0.4	8	

Data presented as mean ± standard deviation, unless otherwise noted.
data displayed is from primary field of irradiation.
* Repeated measures analysis of variance within measures — time group.

Figure 4.1 (Carnaby-Mann et al., 2012) MRI Data.

Table 4.7 Summary of Findings (Kulbersh et al., 2006)

(Kulbersh et al., 2006)				
Identified Physiologic Changes		**Pretreatment Group:**	**Posttreatment Group:**	**P value:**
	n/a			
Quality of Life Outcomes	*M.D. Anderson Dysphagia Inventory* *Unadjusted Scores*			
	Global Assessment	71.7 (62.0–81.3	45.0 (31.3–58.7)	.003*
	Emotional	71.5 (66.0–77.0	57.5 (49.7–65.3)	.005*
	Functional	68.3 (62.4–74.2)	61.3 (53.0–69.7)	.172
	Physical	65.1 (57.8–72.4)	49.0 (38.6–59.3)	.014*
	M.D. Anderson Dysphagia Inventory *Adjusted Scores* (adjusted for age, T-stage site (tonsil and tongue vs. other), follow-up time, treatment, race, and gender)			
	Global Assessment	74.4 (64.5–84.3)	32.9 (17.0–48.7)	.0002 *
	Emotional	72.1 (66.1–78.0	53.9 (44.3–63.5)	.005 *
	Functional	68.7 (62.4–75.1	58.6 (48.5–68.8)	.114
	Physical	66.4 (58.5–74.3)	43.2 (30.6–55.7)	.005 *
Functional Outcomes	n/a			

Table 4.8 Summary of Findings (Carroll et al., 2008)

(Carroll et al., 2008)				
		Pretreatment Group:	**Posttreatment Group:**	**P value:**
Identified Physiologic Changes	Penetration Aspiration Scale	4.11 +/- 2.84	3.88 +/- 2.20	.86
	Posterior tongue base position at rest	26.48 +/- 4.28 mm	32.2 +/- 7.99 mm	.071
	Posterior tongue base position during swallow	15.2 +/- 5.47 mm	22.0 +/- 6.23 mm	.025 *
	Posterior tongue base movement	11.28 +/- 3.69 mm	10.29 +/- 6.56 mm	.70
	Vertical hyoid position at rest	43.73 +/- 5.90 mm	42.8 +/- 7.52 mm	.77
	Vertical hyoid position during swallow	24.97 +/- 6.26 mm	24.96 +/- 5.59 mm	.99
	Vertical hyoid movement	18.75 +/- 4.21 mm	17.84 +/- 8.19 mm	.77
	Epiglottis inversion	89%	33%	.02 *
	Cricopharyngeal opening	8.07 +/- 3.86 mm	7.62 +/- 3.95 mm	.81
Quality of Life Outcomes	n/a			
Functional Outcomes	PEG tube use 12 mo after CRT	33%	44%	.63

CHAPTER 5. DISCUSSION

5.1 Discussion

This review identified and summarized the current available evidence for prophylactic swallowing interventions with a lingual strengthening component for patients with HNC treated with an organ preservation approach. Three publications were included in this review, and all studies evaluated the effects of their respective interventions on the functional swallow.

We assessed three included studies and were unable to conduct a meta-analysis. Studies of a variety of methodological types were included in order to capture the range of evidence that supports prophylactic intervention. Therefore, the quality of some studies included in this review may be weak. Only one study was identified as an RCT (Carnaby-Mann et al., 2012), and it is the only study with a score of greater than 6. In two studies the internal validity was potentially compromised (Carnaby-Mann et al., 2012) as the treatment group was allotted more participant-clinician interaction time than the comparator groups of the studies, potentially increasing the treatment effects. All three studies were conducted at a single institution with small sample sizes. Possible threats to external validity existed in the included studies include the vague descriptions of some exercises and inconsistent follow-up times for outcome measurement. No studies addressed all three domains of physiology, QOL, and function with assessment measures. No studies used the same measure at the same time point. No studies used outcome measures with the objective purpose of measuring lingual strength. One of three studies had data points greater than 1 year post-RT/CRT limiting the comparisons between early and late intervention effects.

Acknowledging the methodological limitations, and heterogeneity of the interventions and outcome measures, we pooled the studies to investigate significant outcomes hypothesized as sensitive to change in lingual strength. Intervention exercises were categorized into five domains: range of motion for jaw, tongue, and larynx, and strengthening exercises for tongue and pharyngeal constrictors, so that we may encourage thoughtful consideration of the components of prophylactic swallowing interventions. Authors examined outcome measures by dividing them into three types: physiologic, QOL, and functional. Outcomes were categorized in attempts to have a more holistic view of the participant and the effects of intervention in multiple domains of life.

The studies demonstrated significant benefit of the treatment through the following measures hypothesized as sensitive to lingual strength: preservation of genioglossus and hyoglossus muscle as determined by T2 MRI; less reduction in MASA scores; improved QOL in three of four domains; maintenance of oral feeding; less use of gastrostomy tube feedings; ability to return to pre-CRT diet without swallow-related complications; and higher "functional swallowing" outcomes. However, no study included direct outcome measures related to lingual strength, such as IOPI. We were unable to access the patient and clinician rated data measures. We can only speculate that with an improved overall score, sub-sections of the measure pertinent to lingual strength may have also improved in rating. For example, the significant results indicated in MASA scores may have been partially attributed to improvements in tongue strength, oral preparation, or oral transit components.

Despite positive results across studies, the effect of an oral tongue strengthening component in a prophylactic exercise protocol on swallowing function for participants with head and neck cancer cannot be determined; nor can we determine the benefit of type and dosage of the lingual strengthening component, or the benefit of proactive versus reactive intervention. We believe this is due to the limited published protocols meeting our criteria, limited patient adherence among studies, and the significant variation among included studies despite a focused research question.

5.2 Study Strengths and Limitations

There were multiple strengths of the current study. The review protocol included a comprehensive search strategy using multiple sources and independent screening of studies for inclusion. Selection, data extraction and risk of bias were independently conducted by each author. The narrow nature of the search strategy facilitated identification of specific intervention strategies aimed at improving or maintaining lingual strength for patients with HNC, which allowed us to identify a more focused set of studies than previous reviews. A focused review highlights the gaps in current evidence and the heterogeneity where limited evidence exists. To gain more information, authors of the included studies were contacted when necessary. Authors comprehensively reported on characteristics of participants, studies, and outcome measures.

This review is also characterized by limitations. We had limited access to databases; specifically, we were unable to utilize EMBASE. At least one proposed protocol applicable to our study was identified as unfinished and unable to be included. Assessment of study quality was limited. No restrictions set for study quality may have resulted in the inclusion of weak evidence. We were unable to conduct a meta-analysis for this review due to small sample size and the heterogenous nature of the articles. Further, we did not collect data on effect sizes, and only qualitatively analyzed results.

CHAPTER 6. CONCLUSIONS

6.1 Conclusions

It can be hypothesized that the benefit of tongue strengthening exercises depends on a number of influencing factors, such as the composition of the exercise protocol, dosage and intensity of the protocol, and overall patient adherence. The effects of lingual exercises may be further investigated in future research.

6.2 Clinical Implications

As described previously, swallowing intervention varies within published studies and in clinical application at hospitals and outpatient settings nationwide. Clinical protocols will continue to vary by agency until a standardized prophylactic swallowing intervention is developed. Until then, we have limited evidence for the care that we are currently providing to these patients.

When considering the components needed for a protocol, specifically a prophylactic exercise program, the nature of the population must be considered. Due to the nature of prophylactic exercises, and the timing of implementation, some patients may have minimal or no swallowing deficits at the time of initiation. Unlike prescribing swallowing intervention reactively, clinicians may not have a VFSS on which to base recommendations on, and the patient's swallowing status is almost certain to decline. Swallowing decline may follow patterns of the population at large, but each patient in this heterogeneous population is different.

The best solution may not be overly cautious prescription of multiple types of exercises in each category, with high intensity and frequency. The author's challenge this popular notion with careful consideration of the HNC population: patient characteristics and history of adherence.

Due to RT/CRT treatment effects, patients experience pain, fatigue, and general discomfort when attempting exercises. Ideally, patients should continue to perform their exercises as directed, but many SLPs encourage patients to do what they can until their discomfort subsides. (Shinn et al., 2013) Unfortunately for the patient and study protocols alike, variations in adherence impacts patient progress and data correlating to the effectiveness of exercises. (Shinn et al., 2013) In the literature few studies measure adherence to prophylactic intervention, and studies that do have different definitions of adherence: at least one set of 10 repetitions per day, for example. Some studies declare adherent or not, while others recognize the partially adherent. Shinn and colleagues conducted a study revealing only 13% of patients were fully adherent while 32% were partially adherent post CRT. In a study by Van der Molen and colleagues (2011), 14% of patients reported to complete exercises on a daily basis during radiation treatment and follow up period, while 57% discontinued all exercises after three and a half weeks. Documented reasons for nonadherence include general lack of understanding of the exercises, radiation side effects interfering with their ability or motivation to perform the exercises, or forgetting to participate. As a result, recent studies with this population, suggest interventions are more likely to be adhered to when they have fewer cycles throughout the day and fewer components. Multiple studies recommend exploration of strategies in future research to improve adherence within this population.

6.3 Research Implications

More research is needed in the area of prophylactic swallowing intervention. Prospective research designs are needed to determine what elements, if any, are necessary to include in a prophylactic protocol. The following tenants must be determined: what exercises to utilize, appropriate dosage, best exercises/dosages for specific types of HNC, timing of intervention in regard to oncologic treatment, assessment measures to use, and timeline of measurement collection.

Before focusing on the dosage and intensity of exercises, researchers must first isolate which exercises are most significantly benefiting these patients (matching the commonly reported deficits of this population) and develop a protocol. Exercises must be specific to the deficit they are aimed to rehabilitate. Further, they must be maximally beneficial; this could be potentially achieved through an efficient dosage, use of the exercise in isolation, or in conjunction with another similar exercise to boost effects. With treatment-associated fatigue and an established risk of adherence, it can be hypothesized that this population would benefit from the least possible number of exercises with the greatest possible benefit.

At least one outcome measure should be sensitive and specific to the variable being manipulated to determine significant change. For example, if treatment arm A uses a protocol with only tongue protrusion strengthening, while treatment arm B uses a protocol with protrusion and lateralization strengthening, an IOPI measure would be more appropriate to measure change than the MASA. Previous studies also recommend that outcomes be consistently measured in the domains of physiology, function, QOL, and patient compliance, and be taken throughout the lifespan of the HNC survivor to adequately evaluate intervention effects. (Greco et al., 2018)

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