Feasibility and Safety of Heavy Lifting Strength Training in Head and Neck Cancer Survivors Post-Surgical Neck Dissection (the LIFTING trial)

By

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ABSTRACT

Background: Despite improvements in surgical neck dissection (ND) procedures, head and neck cancer survivors (HNCS) still endure acute and chronic side effects such as loss of muscular strength, limitations in physical functioning, and fatigue, that impact quality of life and limit return to work. Light-to-moderate intensity resistance training has been shown to improve some of these side effects. Heavy lifting strength training (HLST) has shown promise in further improving outcomes in some populations, but it is unknown if HLST is feasible and safe in HNCS. **Purpose:** The primary aim of the LIFTING trial was to examine the feasibility and safety of a HLST program in HNCS ≥1-year post surgical ND. **Methods:** This single arm feasibility study recruited 8 HNCS to a 12-week HLST program. The 12-week HLST program included 2 training days per week, with a 5 to 8-week progression period towards lifting loads of 80%-90% of 1 repetition maximum (1RM) for bench press, and a rating of perceived exertion (RPE) of 8 to 9 (out of 10) for the squat and deadlift. Accessory movements were also incorporated into the HLST program. The primary feasibility outcomes included the eligibility rate (with reasons for ineligibility), recruitment rate (with reasons for refusal), 1RM testing rate (with reasons for not completing the test), HLST program adherence (including attendance, dose modifications, and progression), and follow-up assessment rate (with reasons for drop out). The primary efficacy outcomes were upper and lower body strength changes from baseline to postintervention. Secondary efficacy outcomes were physical functioning, quality of life, fear of cancer recurrence, pain, anxiety, fatigue, stress, shoulder mobility, sleep, and motivation. Wilcoxon signed rank tests were used to compare the pre-post changes in efficacy outcomes. **Results:** From November 2020 to June 2021 (8 months), 8 participants were recruited to the LIFTING trial. Due to the COVID-19 pandemic, we were unable to track the eligibility rate or recruitment rate, or the associated reasons for not participating. All 8

participants (100%) who were recruited were able to perform the maximal strength tests, and all 8 successfully progressed to heavy loads (80-90% 1RM) at approximately 5-weeks. Median adherence to the 24 supervised HLST sessions was 90.6% (range: 17 (70.8%) to 24 (100%)). Weight lifted from baseline to postintervention increased for the squat/leg press (median change: +36 kg; 95% CI: +25 to +47; p=0.012), bench press (median change: +7 kg; 95% CI: +2 to +10; p=0.012), and deadlift (median change: +13 kg; 95% CI: +6 to +25; p=0.018). In addition, the total weight of the 3 strength exercises combined significantly increased from baseline to postintervention (median change: +55 kg; 95% CI: +40 to +72; p=0.012). Significant improvements were also reported in resting systolic blood pressure (median change: -10.0 mmHg; CI: -17 to -6; p=0.012), resting diastolic blood pressure (median change: -13 mmHg; 95% CI: -16 to -4; p=0.017), resting heart rate (median change: -6 bpm; 95% CI: -10 to -1; p=0.035), and the global health status/quality of life measure (median change: +8.3; 95% CI: 0 to +16.7, p=0.041). No significant changes were observed for physical functioning, fear of cancer recurrence, pain, anxiety, fatigue, stress, shoulder mobility, self-esteem, or sleep quality. Motivational and behavioural outcomes were high at baseline, and remained high postintervention. No adverse events occurred. **Conclusions:** Preliminary results of the LIFTING trial suggest that a HLST program may be feasible and safe for HNCS who are at least 1-year post-ND, and have evidence of recovery of spinal accessory nerve function. Given our recruitment strategy, the eligibility and recruitment rates could not be adequately tracked. HNCS who performed the HLST achieved significant improvements in muscular strength (squat, bench press, and deadlift), resting heart rate, resting blood pressure, and global health status/quality of life. Future research should consider additional recruitment strategies and compare HLST to light-to-moderate load strength training to determine if it is a better prescription for improving outcomes important to HNCS including return

to work. If proven more effective, HLST could be incorporated into the clinical care of HNCS to optimize physical and psychosocial outcomes in this underserved patient population.

PREFACE

This thesis is an original work by Stephanie M. Ntoukas. This research project, of which the thesis is a part, received research ethics approval from the Health Research Ethics Board of Alberta - Cancer Committee (HREBA-CC). Project Name 'Feasibility and Safety of Heavy **LIFT**ing Strength Training **I**n Head and **N**eck Cancer Survivors Post-Sur**G**ical Neck Dissection (the LIFTING trial).'

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CHAPTER ONE

INTRODUCTION

Head and neck cancers (HNCs) are complex and diverse tumours, originating in the oral cavity, oropharynx, hypopharynx, nasopharynx, lip, larynx, paranasal sinus, salivary gland, and mucosal melanoma (1). HNC is the sixth most common cancer worldwide, and makes up approximately 5%-7% of all solid tumours globally (2-4). HNC occurs more often in males - nearly 75% of all cases, with the average age of onset in the 60s (4, 5). Worldwide, there are 650,000 new cases of HNC, and 350,000 deaths every year, with a 5-year overall survival rate of 40%-50% (2, 6). According to the Canadian Cancer Society, 160 females and 440 males (n=600) were diagnosed with HNC in Alberta in 2021.

Standard treatment for early stage HNC is surgery or radiotherapy. Multiple modalities, mainly chemoradiotherapy, are used for locally advanced HNC (7). Despite improvements in treatments, head and neck cancer survivors (HNCS) still endure numerous acute and chronic side effects (7-13). These include dental and oral complications, nutritional, speech and voice impairments, immune suppression, infectious complications, shoulder dysfunction, pain, shortness of breath, weakness, physical fatigue, difficulty sleeping, affected appetite, self-consciousness, embarrassment, unattractiveness, low self-esteem, and reduced quality of life (7, 9, 13-15). Interventions to improve shoulder function, muscular strength, and physical functioning are needed to facilitate return to work and improve overall quality of life.

Strength training has been shown to improve some of these side effects in HNCS. For example, a pilot study examined progressive resistance exercise training (PRET) in 12 squamous cell HNC patients (stage III/IV) undergoing concomitant chemoradiotherapy (16). The trial showed improvements in psychosocial, physical, and dietary intake, with no adverse

events reported that were related to the program (16). In the study, progression in exercise intensity was achieved by having patients advance from 2–3 sets of 15–8 repetition maximum, starting with a low load/high repetition range, to a high load/fewer repetitions per set. Patients trained every other day, 3 times per week, over a 12-week period for a total of 36 sessions; with meal and protein supplements offered at sessions. Results suggested that PRET is safe and feasible in this small sample patient population, with high adherence rates reported (16).

To date, however, most strength training interventions in HNCS have involved light-to-moderate intensity training defined as 2 to 3 sets of repetitions in the 15 (65% of 1RM) to 8 (83% of 1RM) range (16-21). Although effective, HLST programs may provide additional benefits to HNCS for return to work and other usual life roles.

HLST involves lifting loads at 80-90% of 1RM for a total of 3 to 5 sets of 1 to 6 repetitions, with approximately 3 to 5 minutes of rest between sets (22, 23). Some research has shown that HLST programs in adults with no known medical conditions or injuries that may impair training capacity, may produce larger improvements in muscle strength compared to light to moderate strength training (LMST) programs even when controlling for the total volume of work (22, 24). Moreover, loads near maximal (e.g., >85% of 1RM) are required to produce significant increases in strength and 1RM that are not seen with LMST (22, 24). To date, however, there are no studies that have examined the feasibility, safety, and efficacy of an HLST program in HNCS.

The purpose of the LIFTING Trial was to examine the feasibility and safety of a HLST program in HNCS. This thesis consists of four chapters. Chapter One provides an overview of HNCs and their risk factors. Chapter Two reviews the most common HNC risk factors, treatments with a particular focus on neck dissection (ND) procedures, and the associated side

effects, as well as a review of the current literature testing the safety, feasibility, and benefits of weight training in HNCS. Chapter Three (paper) reports the findings of the pilot study examining the feasibility, safety, and preliminary efficacy of HLST in HNCS 1-year post-surgical ND. Finally, Chapter Four provides a general discussion, strengths and limitations of the LIFTING trial, future directions, and conclusions for this thesis.

CHAPTER TWO

LITERATURE REVIEW

HNC

HNC is the sixth most common type of cancer worldwide, and makes up approximately 5%-7% of all solid tumours globally (2-4). Most HNCs are squamous cell carcinomas of the head and neck (SCCHN), originating from the upper aerodigestive tract (3). HNCs begin in the squamous cells that line the mucosal surfaces inside the mouth, nose and throat.

Mutations develop in these squamous cells overtime due to the accumulation of genetic events which are escalated by genomic instability related to the exposure of carcinogenic agents (25). HNC is extremely diverse and complex, with multiple anatomical sites of potential origin (26) including the oral cavity, oropharynx, hypopharynx, nasopharynx, lip, larynx, paranasal sinus, salivary gland, and mucosal melanoma (1). HNCs occur more often in males - nearly 75% of all cases, with the average age of onset being during the sixth decade of life (4, 5). Worldwide, there are 650,000 new cases of HNC, and 350,000 deaths every year, with a 5-year overall survival rate of 40%-50% (2, 6). These cancers are associated with poor clinical outcomes with a 5-year survival rate of 34%-67% depending on the HNC subsite (27). The American Joint Committee on Cancer (AJCC) uses the tumour, node, metastasis (TNM) staging system to classify HNCs and determine the most appropriate treatments. Generally, stage I and II HNC involve small tumours without prominent lymph node involvement (78). Stage III and IV HNCs are characterized by locally advanced disease and invasion of surrounding structures, or greater lymph node involvement with distant metastases (78). In addition, staging oropharyngeal cancers involves the assessment of human papillomavirus (HPV), as HPV-associated (p16+) oropharyngeal cancers are on the rise (78).

HNC Risk Factors

There are several known risk factors for developing HNC. Tobacco use (whether smoked, chewed, or inhaled) and alcohol consumption are the strongest independent risk factors responsible for increasing one's risk of HNC, along with HPV associated with sinus, nasal, and oropharyngeal cancers (2, 26). Alcohol and tobacco use contribute to the etiology and risk factors of HNCs originating in the oral cavity, oropharynx, and hypopharynx (1). Smoking is associated with post-treatment complications and adverse effects on oncological outcomes, and continued alcohol consumption has negatively impacted survival rates (26). It has also been demonstrated that tobacco use is associated with an increased risk of surgical site infection (8). It is estimated that 90% of all HNCs are diagnosed in people who smoke tobacco alone or with alcohol, and smokers have a 5-10 times higher risk of developing HNC in comparison to lifetime non-smokers (2). In addition, the risk for developing laryngeal cancer is 20 times higher in heavy smokers versus lifetime non-smokers (2). Furthermore, smoking is correlated with a reduction in lower body muscle function, which may be related to reduced skeletal muscle oxidative capacity, blood flow, and strength in HNC patients (28). The longer these detrimental lifestyle behaviours continue, the greater the risk of developing HNC. Other risk factors include poor oral hygiene, low intake of fruits and vegetables, infection with the Epstein-Barr virus, and DNA from HPV (2). HPV infection is a risk factor contributing to the development of HNCs of the oropharynx (lingual and palatine tonsils, and base of tongue) (1). Smoking, alcohol consumption, and infection with HPV are the most common risk factors for developing HNC, which may also be associated with physical inactivity (28). Patients who are immunosuppressed due to poor nutrition, advanced age, immunosuppressive therapy post-transplant or due to acquired immunodeficiency syndrome are also at an increased risk for developing HNC (26).

HNC Treatments

Standard treatment for early stage HNC is surgery or radiotherapy (7). Patients with locally advanced HNC require multiple treatment modalities, mainly chemoradiotherapy (7). However, some patients require induction chemotherapy, followed by cetuximab radiotherapy, chemoradiotherapy, or surgery (7). Unfortunately, HNC treatments, especially surgical interventions, are associated with debilitating acute and chronic side effects such as dental, nutritional, speech impairments, voice impairments, and shoulder dysfunction (7, 9). Moreover, NDs are also independently associated with an increased risk of a surgical site infection occurring within 30 days of surgery or within a year following dental implants (8). All treatment modalities - radiation therapy, surgery, and neoadjuvant, adjuvant, and/or concurrent chemotherapy result in oral complications in HNCS (13). Radiation- and chemotherapy-induced neuropathies are associated with inflammatory/infectious complications, physiological changes, and immune suppression during and after treatment, which can be improved with good oral hygiene and nutrition practices, reduction of alcohol and tobacco use (13), and potentially with the introduction of an exercise intervention.

HNCs are treated with surgery in the form of a ND with or without reconstruction, radiation, chemotherapy, or any combination of the three methods (25). Surgery and radiation are the primary treatment options for most HNC patients, despite their association with severe side effects and significant morbidity (76). The surgical ND was the standard of care technique used in the management of HNC over the past century (30). The extremely invasive ND may involve the removal of the sternocleidomastoid muscle (SCM), spinal accessory nerve (SAN), and/or internal jugular vein (IJV) (31). SAN injury commonly occurs during ND surgery for HNCs. Although modifications have been made to this surgical procedure, HNCS still experience impairments in

muscular strength and active range of motion of the neck and shoulder in comparison to healthy controls (32). For instance, a literature review demonstrated that up to 67% of patients who underwent any variation of a modified ND (modified radical or selective ND) experienced similar symptoms to those who had a full ND, such as shoulder dysfunction and pain (33). Due to the invasive nature of the surgery, a long recovery time is necessary for muscles and nerves to heal from treatment-related effects. Although recovery is unlikely, neurotmesis (nerve damage) of the SAN may occur when nerve grafting is performed. SAN recovery and trapezius reinnervation mainly occurs between 4 and 6 months, but may improve beyond 1-year post-ND (77). The majority of shoulder function (abduction) begins to recover within the first 6 months post-ND, and may also continue to slowly improve for 1 or more years post-surgery (77). HNCS also experience a significant depletion in skeletal muscle posttreatment which impacts their survival, quality of life, response to cancer treatment, and increases the risk of postoperative complications (34).

Neck Dissection Side Effects

The SAN provides motor innervation to the trapezius and SCM (12). These muscles act to elevate the shoulder, stabilize scapula, extend neck; rotate and flex the neck respectively (12). Surgical-ND injury to the SAN results in trapezius paralysis or dysfunction and a diagnostic cluster of signs and symptoms, including trapezius atrophy, shoulder girdle depression, scapular dyskinesis, loss of shoulder active abduction, and most commonly, shoulder and neck pain and dysfunction (11, 12). SAN injury can result in limited active shoulder range of motion and functional deficits. Other scapular muscles may compensate for the lack of trapezius involvement in shoulder movement, which may help compensate for restricted shoulder flexion range of motion.

Nowadays, the SCM is most often spared in ND procedures. However, shoulder dysfunction may be present in as many as 50% to 100% of patients who have had a ND, amongst multiple other side effects (9). Several other patients demonstrated SCM paralysis post-surgery (11). Identifying patients with a SAN injury post-ND is crucial because poor outcomes may result if early physical therapy is not initiated (11). For example, decreased shoulder flexion and abduction is associated with reduced quality of life in 5-year HNCS (10). Pain and dysfunction are associated with loss of innervation of SAN due to 'shoulder syndrome' post-ND for cervical metastasis (12). Shoulder syndrome can be defined as 'shoulder droop' - winged scapula (abnormal protruding of the shoulder blades), an inability to shrug and a dull, non-localized pain (12). Although the function of the trapezius is compromised post-ND, reinnervation of the muscle may significantly improve 6 months post-surgery and may result in greater active range of motion (11). However, not all HNCS gain trapezius function even if the SAN is spared, and HNCS can expect a long recovery period.

It was reported that 69% of patients with SAN dysfunction had pain complaints at 3-years following ND surgery (11). All patients who underwent a ND in this series complained of neck and/or scapular pain (11). Additionally, job loss is also a concern in this group as HNCS are 1.4 times more likely to become unemployed and struggle to return to work when compared to healthy controls (36). As a whole, 25%-50% of HNCS will become unemployed after diagnosis (37). Moreover, a study that involved 74 HNCS examined quality of life post-ND. The authors reported that regardless of the extent of ND performed, all 74 HNCS experienced neck stiffness, constriction, and complaints about appearance, with all variations of surgery producing fibrosis in the neck (35). Patients with chronic disease should implement resistance exercises into their

rehabilitation programs, with special attention paid to cancer patients who will display with skeletal muscle wasting, which increases mortality and morbidity risk (39).

Exercise Interventions in HNCS

Exercise has been tested as an intervention to improve health-related fitness and patient-reported outcomes in HNCS. To date, 10 studies (14, 16, 19, 40-45, 75) have examined the role of exercise interventions in HNCS (see **Table 5**).

Overall, the randomized controlled trials, randomized crossover trials, comparative designs, case reports, or pilot studies that were conducted recruited between 3 and 52 HNCS. The participants that engaged in various resistance training exercise protocols demonstrated positive results such as improved fitness, physical functioning, symptom management, tiredness, quality of life, and excellent completion and adherence rates (14, 16, 19, 40-42, 44, 45). In addition, results showed that progressive strength training is safe and feasible in this cancer population (14, 16, 19, 40-45). General limitations of these studies included: small sample sizes, wide range in participant age and time since treatment to start of the intervention, diverse cancer site, lack of long term follow-up data, and self-reported physical activity (14, 16, 19, 40-45, 75).

One systematic review involving 16 articles summarized all available exercise literature in HNC patients as of 2014 (46). Despite the heterogeneity in exercise frequency, intensity, time, type, duration, outcomes, and assessment tools of the studies, the results were promising in terms of exercise in HNC populations both during and post chemotherapy and/or radiation, or surgery alone. The systematic review demonstrated that exercise was safe and feasible, and may lead to improvements in muscular strength, lean body mass, physical function, fatigue management, and quality of life (46).

In a prospective pilot study, progressive resistance exercise training (PRET) was examined in 12 squamous cell HNC patients (stage III/IV) undergoing concomitant chemoradiotherapy (16). Progression in exercise intensity was achieved by patients advancing from 2–3 sets of 15–8 repetition maximum, starting with a low load/high repetition range, and then progressing to a high load/fewer repetitions per set. Patients trained every other day 3 times per week, over a 12-week period of 36 sessions; with meal and protein supplements offered at sessions. Psychosocial and physical improvements were reported in this group (16). Benefits were also reported in HNCS (stages I-IV) that were on or had completed radiation or concurrent chemo-radiation treatment (14). This randomized controlled trial involved a 12-week progressive strength training program, 3 days per week (14). Participants completed 10 full body exercises, and 2 sets of 8-10 repetitions at moderate intensity (14). The trial demonstrated that progressive strength training for HNCS is feasible, and showed significant improvements in fitness and physical functioning outcomes, improvements in symptom management, tiredness, and drowsiness (14).

In a randomized controlled trial with 52 HNCS involving PRET, significant reductions in shoulder pain and disability, as well as improved upper extremity strength and endurance were found (19). In the trial, intervention participants were prescribed 2 sets of 10 to 15 repetitions involving 5 to 8 upper extremity exercises beginning at 25% to 30% of 1RM, then slowly progressed to 60% to 70% 1RM by the end of the 12-week intervention period (19). Finally, PRET slightly improved shoulder pain, shoulder disability, active range of motion for external rotation, passive range of motion for abduction, forward flexion, external rotation and horizontal abduction in HNC patients (9).

Overall, the literature suggests that exercise, especially strength training, is an effective intervention for improving health-related fitness, physical functioning, and quality of life in

HNCS. Although HLST might sound suitable for those wanting to return to their physically demanding jobs, it is unclear what the optimal strength training prescription is for HNCS (46). The studies to date have tested what would be considered 'light-to-moderate' strength training interventions such as 1 to 2 sets of 25 repetitions (43), to 2 to 3 sets of repetitions performed in the 8 (≥60% of 1RM) to 15 (83% of 1RM) range (14, 16, 19, 40-42, 44, 45). It is possible that heavier weight training loads may produce even better outcomes for HNCS.

HLST Overview

Strength can be described as the maximum force or tension that a single muscle or group of muscles can produce with one contraction or repetition (47). There are multiple terms used in the literature to describe the concept of resistance training with heavy loads such as 'heavy load lifting,' 'heavy resistance training,' and 'high intensity resistance training.' Additionally, there is also variability in the number of sets and repetitions applied to a heavy load strength program; typically, around 3-5 sets of 1-6 repetitions, depending on the literature source under review. For the purposes of my thesis, the term 'heavy load strength training' (HLST) was used to describe lifting loads of 80%-90% of 1RM or an RPE of 8-9 on the 10-point Borg-CR10 Scale (81), for 3-5 sets of 1-6 repetitions for each main exercise (squat, bench press, and deadlift).

HLST in the general population has been examined much more frequently than in cancer populations. A meta-analysis of 15 studies was conducted which compared the efficacy of heavy and light-moderate load resistance training to no exercise in people (50 years or older) in order to assess changes in muscle size and strength (48). The review defined high-intensity resistance training as a progressive increase in loads to 80% of 1RM or higher, and low-moderate intensity resistance training was defined as training loads that averaged a maximum of 60% of 1RM or lower (48). Training was performed three times per week in all studies with participants

performing higher (78.8-82.8% of 1RM) and lower intensities (35.4%-53.4% of 1RM) (48). Overall, the review demonstrated greater changes in muscle strength across all studies with high-intensity resistance training (48). In addition, all studies under review found that training with higher intensities of load was more effective in encouraging increases in muscle size (hypertrophy) (48). Although both heavy and light-to-moderate load resistance training programs can similarly increase muscle strength (43% and 35% respectively) in elderly populations when matched for mechanical work as compared to non-training controls, training with loads of 80% 1RM or higher results in greater strength gains (48). This meta-analysis suggests that training with heavy loads may optimize strength gains, with a blunted ability to gain muscle in elderly populations (48).

Another systematic review and meta-analysis of 21 studies showed similar findings (24). Its purpose was to review current literature in order to compare changes in strength and hypertrophy between low versus high load resistance training protocols lasting a minimum of 6-weeks in adults ages 18 to 65+ years (24). Low load training was defined as training intensities of 60% 1RM or lower, and high load training was defined as training intensities greater than 60% 1RM (24). Although this review demonstrated that muscle hypertrophy can be achieved with a wide range of applied loads, gains in muscle strength were significantly greater with high loads versus low loads (24). The review also mentioned that low loads may require more time to complete exercises with sufficient training volume to elicit change; therefore, suggesting that high load training may be more time efficient (24).

The most recent systematic review and network meta-analysis of 28 studies analyzed the effect of resistance training performed to volitional failure with low (<60% 1RM), moderate (60-79% 1RM), and high loads (≥80% 1RM) on muscle strength and hypertrophy in 747 healthy men and women, with a mean age of 23.4 years. Effects on muscle strength were load dependent, with

higher loads resulting in greater strength improvements in a short period (average of 24.6 training sessions over 8.9 weeks) (49). On the contrary, improvements in muscle hypertrophy seem to be load independent, with hypertrophic responses elicited using varying loads in untrained and recreationally trained individuals, not strength athletes (49).

In a study that involved untrained elderly men between the ages of 60 and 75 years old in a 16-week high intensity (85%-90% of 1RM) resistance training program consisting of 2 sessions per week, and 3 sets to failure of 6-8 repetitions for 3 lower body exercises was performed (52). Improvements in peak aerobic and maximal working capacities, significant strength gains, considerable hypertrophy, and minimal changes to serum lipid profiles were reported (52). The effect of a 42-week progressive weight lifting training program on muscular strength, muscle size, bone mineral density, peak power output in cycle ergometry, and symptom limited endurance in walking and stair climbing was examined (53). One hundred and ninety three apparently healthy participants between 60 and 80 years old with no prior resistance training experience, who performed upper and lower body exercises; 10 and 12 repetitions respectively (50-80% 1RM) were examined (53). In the absence of injury, resistance training is safe and appropriate for older adults, and the exercise intervention resulted in 20-65% increases in 1RM strength, with dynamic strength continuing to increase even after the 42-week intervention period (53). Small but significant improvements in peak power were made, as well as an increase in treadmill endurance and stair climbing (53). On the other hand, there were no changes reported in measurable bone remodelling in healthy seniors (53). The trial concludes that regular weight training in the elderly is a great tool for potentially preserving independence and improving quality of life (53). Lastly, a meta-analysis was conducted in elderly populations with a mean age of 67.8 years old, involving resistance training 3 times per week (48). Results demonstrated that when total physical work is

matched, both heavy (~80% 1RM) and light to moderate loads (~45% 1RM) can produce strength, but heavy loads may be required to maximize strength gains (48). However, this meta-analysis compared on average 8 repetitions (heavy loads) with 16 repetitions (light to moderate loads). Of the 15 studies reviewed, only 3 studies involved heavy loads under 8 repetitions. The results of this meta-analysis may have been more significant if additional studies were included which implemented heavy load training.

Currently, there are three papers that are particularly relevant to the design of the proposed study intervention **(Table 4)**. A randomized crossover trial involving low loads (60%-65% of 1RM), and 2 sets of 15-20 repetitions; in addition to heavy loads (85%-90% of 1RM), and 3 sets of 5-8 repetitions was conducted in 21 newly diagnosed breast cancer patients receiving adjuvant chemotherapy with a prior axillary lymph node dissection (50). The authors examined the impact of heavy load lifting on the lymphatic system. Results of this study demonstrated a similar lymphatic response when using low or high loads, but less swelling at 72 hours post exercise in women with axillary node dissection at risk for lymphedema during adjuvant chemotherapy (50).

The second study was a randomized controlled trial, and implemented a heavy load, lower body exercise program in 55 newly diagnosed breast cancer patients scheduled for adjuvant therapy. It demonstrated improvements in lower extremity muscle strength, walking economy, functional performance, overall quality of life, and the maintenance of muscle mass after a 12-week strength training program consisting of 4 sets of 4 repetitions of the leg press at ~90%, twice weekly (51). These results were compared against the control group, which performed 3 sets of 10 chair rises 2 times per week, over a 12-week timespan and displayed reductions in all measured variables. The lower body, heavy load exercise program using the leg press machine was deemed safe and feasible for this patient group (51).

The third study was also a randomized controlled trial, and implemented a machine-based PRET program in 37 prostate cancer patients on androgen deprivation therapy. The exercise intervention took place 3 days per week, for a total of 12 weeks, and progressed from 60% 1RM for 15 repetitions to 83% 1RM for 8 repetitions (17). The authors reported improvements in sarcopenia, body fat percentage, strength, and quality of life postintervention (17).

Summary and Conclusions

MLST programs have been shown to improve outcomes in HNCS. Research in other populations suggests that HLST may produce better outcomes than MLST. Currently, there is no literature examining the effects of a HLST program in HNCS or patients, and this is a significant knowledge gap. The first step of the LIFTING trial was to confirm the safety and feasibility of HLST in the HNC group. This study has challenged current beliefs which advise HNCS to take a cautious approach to exercise or avoid it completely (50). Therefore, the LIFTING trial examined the feasibility and safety of a HLST in HNCS at least 1-year post-surgical ND.

CHAPTER THREE

PAPER

Feasibility and Safety of Heavy Lifting Strength Training in Head and Neck Cancer Survivors Post-Surgical Neck Dissection (the LIFTING trial)

Introduction

Standard treatment for early stage HNC is surgery or radiotherapy. Multiple modalities, mainly chemoradiotherapy, are used for locally advanced HNC (7). Despite improvements in treatments, head and neck cancer survivors (HNCS) still endure numerous acute and chronic side effects (7-13). These include dental and oral complications, nutritional, speech and voice impairments, immune suppression, infectious complications, shoulder dysfunction, pain, shortness of breath, weakness, physical fatigue, difficulty sleeping, affected appetite, self-consciousness, embarrassment, unattractiveness, low self-esteem, and reduced quality of life (7, 9, 13-15). Interventions to improve shoulder function, muscular strength, and physical functioning are needed to facilitate return to work and improve overall quality of life.

Strength training improves some of these side effects in HNC survivors (HNCS). One systematic review involving 16 articles summarized all available exercise literature in HNC patients as of 2014 (46). Despite the heterogeneity in exercise frequency, intensity, time, type, duration, outcomes, and assessment tools of the studies, the results were promising in terms of exercise in HNC populations both during and post chemotherapy and/or radiation, or surgery alone. The systematic review demonstrated that exercise was safe and feasible, and may lead to improvements in muscular strength, lean body mass, physical function, symptom management, and quality of life (46).

Prior exercise oncology literature suggests that most exercise interventions have been conducted in HNCS using light to moderate intensity ranges. However, strength specific research suggests that training with heavy loads may be required to maximize strength gains (24, 48). This raises the important question of whether a HLST exercise program has even greater benefits for HNCS such as improving quality life and increasing muscular strength.

The primary purpose of this single arm study was to test the feasibility and safety of a HLST program in HNCS at least 1-year post-surgical ND. A secondary purpose was to examine the preliminary efficacy of HLST for improving muscular strength, physical functioning, quality of life, post traumatic growth, fear of cancer recurrence, pain, body composition, anxiety, fatigue, stress, shoulder mobility, self-esteem, sleep, and motivation to engage in a HLST. We hypothesized that HNCS who have undergone a surgical ND would be willing and able to participate in a HLST program. We also hypothesized that there would be increases in muscular strength and patient-reported outcomes from baseline to post intervention.

Materials and Methods

Setting and Participants

This study was conducted at the University of Alberta in Edmonton, Alberta, Canada. This study received ethics approval by the Health Research Ethics Board of Alberta Cancer Committee (HREBA-CC). HNCS were recruited from: a) a HNC surgical clinic at the University of Alberta Hospital, b) the Cancer Rehabilitation Clinic in the Faculty of Rehabilitation Medicine at the University of Alberta, c) the Head and Neck Cancer Support Society, and d) self-referral from HNCS who heard about the LIFTING study.

Eligibility criteria included: 1) previously diagnosed with any subtype and stage of HNC including thyroid cancer; 2) at least 1-year post-ND for HNC with full shoulder range of motion or recovery of the SAN as deemed adequate by physical examination; 3) adults ages 18 and up; 4) no unmanaged medical conditions, alcohol, or drug abuse; 5) approved for a HLST program by the treating surgeon and a certified exercise physiologist; and 6) ability to understand and communicate in English. Participants were excluded if they were currently involved in an exercise trial (aerobic, strength, or combined) or a clinical drug trial.

Design and Procedures

This single arm study involved assessments before and after the 12-week HLST intervention. Between November 2020 and June 2021 (8 months), potentially eligible HNCS were identified and screened for eligibility by a nurse and physiotherapist during follow-up visits and rehabilitation sessions. HNCS were put in touch with the study coordinator via email and/or phone for more information about the study. Interested HNCS met with the study coordinator via an online pre-screening meeting, which served as a chance to ask about medical history, elaborate further on study details, and obtain written informed consent. Once online questionnaires were complete in the Research Electronic Data Capture (REDCap), the study coordinator scheduled interested HNCS for in-person baseline physical assessments at the Behavioural Medicine Fitness Centre at the University of Alberta. Finally, eligibility was determined through objective measurements of shoulder flexion and abduction range of motion. To satisfy all eligibility criteria, participants were required to meet or exceed the following age-based cut points for shoulder range of motion: participants 18-50 years old: ≥150° for flexion and abduction; participants over 50 years old: ≥130° for flexion and abduction.

Maximal Strength Testing

Three 1RM tests were used for baseline and postintervention physical assessments to evaluate upper and lower body strength in the barbell squat, bench press, and deadlift. Prior to attempting these movements with the barbell, the study coordinator gave an in-depth explanation of the purpose of the tests, how to safely execute the lifts, and demonstrated the movements. If participants were not able to safely execute the strength movements with a wooden dowel after multiple attempts, the following substitutions were planned for the duration of the 12-week

intervention: leg press to replace the barbell squat, dumbbell bench press to replace the barbell bench press, rack pulls or dumbbell deadlifts to replace the barbell deadlift from the floor.

To begin, after a 5-minute aerobic warm up and standardized dynamic stretches, study participants performed bodyweight movements and used a wooden dowel to practice appropriate movement techniques. Progressions leading up to the 1RM were as follows. For the squat and deadlift, participants initially performed 8-10 reps with the empty barbell. To follow, the reps decreased as the weight gradually increased based on body weight in pounds: 50% body weight for 5-6 reps, 70% for 2-3 reps, and 85%, 90%, 95%, and 100%+ for 1 rep. For the bench press, after practicing with the wooden dowel, progressions leading up to the 1RM may have begun with dumbbells or the empty barbell for 8-10 reps. Following this, the reps also decreased as the weight gradually increased based on body weight in pounds: 35% body weight for 5-6 reps, 40% for 2-3 reps, 45% and 50%+ for 1 rep. 1RM tests were performed in this order: squat, bench press, deadlift.

In order to assess actual 1RM, the following factors were considered. Since the Borg RPE Scales are primarily used to assess intensity of aerobic exercise and may be inaccurate and difficult to conceptualize for beginner lifters (80), a repetitions in reserve (RIR)-based RPE scale was used to assess exercise intensity, which may be more valid to assess maximal or near maximal strength. After each set during the physical assessments, participants were asked for their RPE, which corresponded to a number on the RIR scale. Participants were asked the following question, "If I didn't stop you, how many more repetitions could you have done after the prescribed number?" Conversions from RPE to RIR are as follows: RPE 10=RIR 0 (maximum effort), RPE 9=RIR 1, RPE 8=RIR 2…RPE 1=RIR 9+ (little to no effort) (80). For 1RM testing, participants

should have reported an RIR of 0-1, or RPE of 9-10, in order for the lift to be considered close to or a true maximal test.

In addition to the RIR-based RPE reports, observation by the study coordinator was used to assess actual or peak 1RM tests. As the weight increased and the reps decreased while approaching a 1RM, time under tension (total duration of lift) should have been progressively longer. Participants should have been somewhat struggling to get the weight up when a true maximum was reached, and not easily lifting the barbel. If the latter was the case and participants did not want to continue for whatever reason, the reps and load were plugged into a 1RM prediction equation.

Finally, form was paid close attention to for all 1RM test. Participants should have maintained the same squat depth even as loads were increased, although there is a tendency to shorten range with increasing weight, making the lift easier and shorter in duration (less time under tension). If squat depth was progressively shortened or heels were no longer flat on the floor with increasing load, the lifter was reminded to squat lower and push the weight through the back half of the foot (heel) if possible, or they were stopped if this was not possible. In addition, if the bench press range was shortened with increasing weight (started touching chest but no longer does), the lifter was reminded to lower the barbell more, adjust grip, or they were stopped if the same form was not possible to maintain. Lastly, for the deadlift, if the lifter was able to maintain a flat back with lighter loads but no longer with heavier loads, they were reminded to push through the legs, squeeze glute muscles, and to imagine the shoulder blades reaching down towards the back pockets to keep the barbell close to the body. They were stopped if this was not possible and the lower back continued to round. Once 1RM tests were complete, 5-10 minutes of standardized static stretches were performed.

Exercise Intervention

Participants in the study took part in a 12-week, supervised, HLST exercise program 2 days per week, while progressively working towards lifting loads of 80%-90% of 1RM for bench press, and an RPE of 8 to 9 for squat and deadlift. The justification for the exercise frequency of 2 days per week was from a study examining the motivational effects of resistance training 3 versus 2 days per week in prostate cancer survivors (54). The 3 days per week group perceived less support, more difficulty, and less benefit for self-esteem, physical functioning, fatigue, cardiovascular endurance, and happiness (54). Overall, the group engaging in resistance training 3 days per week perceived more barriers to the program which included feeling sick, travelling to the fitness centre, and other medical conditions (54). We expected adherence and retention rates to be higher with a frequency of 2 days per week, which would allow for sufficient time between sessions for a full recovery.

Prior to each exercise session, participants were guided through a 5-10 minute warm up. This consisted of low-intensity biking or walking for 5 minutes, and dynamic movements such as: leg swings, arm circles, hip, shoulder, and ankle mobility. At the end of each session, participants were guided through a 5-10 minute cool down. This consisted of static stretching. For the HLST intervention, exercises consisted of 3 main movements (squat, bench press, and deadlift), as well as accessory/auxiliary movements (face pulls, pushups, dumbbell lunges, farmers carry, and planks). There was an individualized 5 to 8-week progression/adaptation period to heavy loads (80%-90% of 1RM) which depended on the patient's experience with weight training, ability to safely execute movements, RPE, and their performance on the baseline strength and functional measures. For safety purposes, measurements of heart rate and blood pressure were taken before each session, and questions regarding fatigue and pain were asked before and after each session.

The HLST exercise intervention included bench press, but no overhead pressing movements because overhead exercises have been associated with higher levels of trapezius muscle activity in patients with SAN injury following ND surgery (41), and loaded overhead exercises might have caused pain or discomfort with a lack of trapezius activation and poor scapular positioning. Each main movement was performed for 1-6 repetitions (80%-90% of bench press 1RM, and an RPE of 8-9 on the 10-point Borg CR-10 Scale for squat and deadlift), for a total of 3-5 sets. Once the 3 main exercises were performed for 6 repetitions or less, rest periods of 3-5 minutes between sets were required. Just like with 1RM testing, after each set during exercise sessions, participants were asked, "If I didn't stop you, how many more repetitions could you have done?"

Auxiliary or accessory movements are a single joint exercise targeting specific smaller muscle groups (55), which were also included in the training protocol in addition to the 3 main movements. For example, planks, pushups, leg extensions, leg press, lunges, face pulls etc. Auxiliary movements target smaller muscle groups in comparison to multi-joint compound exercises which target multiple larger muscle groups. In addition, they place less of a demand on the body, and should ideally be performed after compound lifts, which are more demanding. Intensity of the 3 primary movements was based on 1RM and RPE. To progress the intensity, it has been recommended that a 2–10% increase (lower percent for small muscle mass exercises, higher percent increase for large muscle mass exercises) in load be applied when the individual can perform the current workload for one to two repetitions over the desired number for two consecutive training sessions (56). Total volume (sets x reps x load) was increased if heavy loads were tolerated well (i.e., participants reported >1 RPE less than the predicted RPE for two consecutive sessions). Once participants reached heavy loads (80% 1RM), total volume was

gradually progressed at this intensity by increasing reps and sets, before increasing intensity to 85%, then progressing to 90% 1RM. Sets and reps were progressed within our defined parameters (3-5 sets and 1-6 repetitions) before intensity was increased.

Demographic, Behavioral and Medical Characteristics

Demographic and behavioral variables were assessed using self-report. Baseline exercise was assessed with the Godin Leisure Time Exercise Questionnaire (GLTEQ) (57). Medical data was extracted from medical records which included: type of HNC, type of ND, type of treatment, cancer recurrences if any, other medical conditions, current and previous injuries, and a list of medications.

Health-Related Fitness Outcomes

Health-related fitness outcomes were assessed at baseline (within 1-week prior to starting the HLST program) and at postintervention (within 1-week of completing the HLST program). 1RM was used as the strength measure for bench press as this movement requires smaller muscles and is typically less demanding on the body in comparison to the squat or deadlift. RPE was used to measure lower body strength in the squat and deadlift, and may be the optimal measure of strength in terms of safety, reliability, validity, and tolerability (58). The 1RM test is a reliable and simple method to evaluate maximal strength of resistance exercises in 'healthy' men and women, and it can be used by athletic trainers, health and fitness professionals and rehabilitation specialists to quantify the level of strength, to assess strength imbalances, and to evaluate training programs (59). 1RM and RPE scale are equally effective at improving muscular strength and functional performance in an older population (58), and we expected the majority of participants to be of middle to older age due to the age of onset of HNC. Body composition was assessed using hip to waist ratio, height, and weight. Additional functional fitness assessments for participants 50 years

and up included: 6 Minute Walk Test (6MWT), and 30 second sit to stand (51). Shoulder flexion and abduction ranges of motion were measured using a goniometer to ensure ranges met the cut points required for study eligibility outlined above.

Patient-Reported Outcomes

Patient-reported outcomes were assessed at baseline (within 1-week of starting the HLST program) and at postintervention (within 1-week of completing the HLST program). These variables were assessed by questionnaires completed on REDCap. Quality of life was measured using the European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire-C30 (EORTC QLQ-C30) (60). Post traumatic growth was assessed using the Post Traumatic Growth Inventory (PTGI) (61). Fear of cancer recurrence was measured using the Fear of Cancer Recurrence Inventory (FCRI) (62). Cancer specific quality of life was measured using the well-validated Functional Assessment of Cancer Therapy-Head and Neck (FACT-H&N Symptom Index) (63). Anxiety was measured using the Spielberger State Trait Anxiety Inventory (STAI) (64). Fatigue was assessed using the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) questionnaire (65). Perceived stress was measured using the Perceived Stress Scale (PSS) (66). Impairment as a result of the cancer treatment of the neck was measured using the Neck Dissection Impairment Index (NDII) (67). Symptom burden including pain, tiredness, nausea, depression, anxiety, drowsiness, appetite, overall wellbeing, and shortness of breath was assessed using the revised 9-item Edmonton Symptom Assessment System (ESAS-r) (68). Self-esteem was measured using the Rosenberg Self-Esteem Scale (RSE) (69). Typical sleep habits were measured using the Insomnia Severity Index (ISI) (70).

Motivational Predictors/Outcomes

Motivational questions derived from the Theory of Planned Behaviour were asked about the HLST program. At baseline, participants were asked questions about how they felt about doing the supervised HLST program. These questions were on a 5-point scale ranging from 1 (not at all) to 5 (very much) and included how beneficial, enjoyable, and difficult they thought the program would be, anticipated support from family/friends, perceived control over the program, and their confidence to complete the program. At postintervention, participants were asked to retrospectively evaluate the HLST program using the same items in the baseline questionnaire (e.g., how enjoyable was the program). They were also asked to evaluate a list of benefits and harms on a 7-point scale ranging from -3 (worse) to +3 (better) and a list of barriers on a 7-point scale ranging from 1 (not at all) to 7 (very much). Finally, participants were asked how they felt about doing a HLST program over the next 6 months on their own on a 5-point scale ranging from 1 (not at all) to 5 (very much). Items addressed were identical to those assessed during the baseline questionnaire, and included benefit, enjoyment, support, motivation, difficulty, controllability, and confidence to complete a HLST program on their own. A final question was asked regarding whether or not participants had a detailed plan in place to carry out the HLST program on their own over the next 6 months.

Statistical Analysis

For this single arm feasibility and safety study, our goal was to recruit 15-20 HNCS over a 6 month period. With 16 HNCS, we would have had 80% power to detect a large standardized effect size of 0.80 standard deviations and a two-tailed alpha of $p<0.05$ for the efficacy outcomes. Descriptive analyses were used to quantitatively report the eligibility rate, recruitment rate, adherence rate, assessment rate, attrition rate, and adverse event rate. Preliminary efficacy analyses

examined changes from baseline to post intervention in muscular strength and patient-reported outcomes using Wilcoxon signed rank tests.

Results

Recruitment Rate and Baseline Demographic/Health Characteristics

The flow of participants through the LIFTING trial is presented in **Figure 2.** From November 2020 to June 2021 (8 months), 14 potentially eligible and interested HNCS were referred by clinic staff to the study coordinator for further review. Due to the COVID-19 pandemic and staff redeployment and suspension of in-person recruitment, we were unable to track how many HNCS in the two clinics were screened, deemed ineligible, approached, or declined. Of the 14 potentially eligible and interested HNCS referred to the study coordinator, 2 were unable to be contacted after multiple attempts, 1 declined because of a rotator cuff injury, 1 was deemed ineligible because of unmanaged comorbid disease, 1 was deemed ineligible due limited shoulder range of motion, and 1 did not provide the required medical clearance. No HNCS were self-referred from the support group, word-of-mouth, or referred from the Otolaryngology Head and Neck clinic at the University of Alberta. In total, 8 HNCS were recruited to the study.

The baseline demographic, behavioural, and medical characteristics of the 8 participants are reported in **Table 6.** The mean age of participants at baseline was 65.6 years (range: 57-81 years), which included 7 males (87.5%) and 1 female (12.5%). All 8 participants (100%) completed college/university or above. The average BMI was 25.6 kg/m^2 (SD: 0.9), and no participants were obese (>30.0 kg/m^2). In terms of current exercise, 4 participants (50%) were engaged in aerobic exercise only; 3 (37.5%) were engaged in aerobic and resistance exercise, and 1 (12.5%) reported no exercise.

In terms of the primary HNCs, 5 (62.5%) had tongue/base of tongue, 1 (12.5%) oropharynx, 1 (12.5%) larynx, and 1 (12.5%) unknown primary. The mean time since surgery was 7.5 years (range: 2-17 years). Seven participants (87.5%) were current or ex-drinkers, and 4 participants (50%) were current or ex-smokers. In addition to surgery, all 8 participants (100%) received radiation therapy, 4 (50%) received chemotherapy, and 1 (12.5%) received biological/hormone/targeted therapy.

Feasibility of Maximal Strength Testing

All 8 participants (100%) attempted the baseline maximal strength testing. Issues and challenges that were experienced during baseline maximal strength testing are summarized in **Table 7.** On average, the duration of baseline testing was 2.16 hours. All 8 participants (100%) were able to attempt all three maximal strength tests, but some modifications were made. Two participants (25%) were unable to safely perform an empty barbell squat due to lower body donor site location discomfort or instability. These participants used the leg press instead for the baseline maximal test. Three of the 6 participants (50%) who performed barbell squats preferred to squat with a folded towel on upper back for comfort. Two participants (25%) were unwilling to complete a 1RM for one exercise each, one for the squat and one for the deadlift. Instead, a 3RM and 2RM were performed respectively, and a 1RM calculation was applied to develop their exercise prescriptions. The same 1 participant (12.5%) who performed a 3RM squat, did not perform a true maximal test based on observation. Additionally, 1 participant (12.5%) did not touch their chest with the barbell during the bench press due to restrictions in external shoulder rotation. Another participant (12.5%) did not touch their chest during the bench press in order to avoid shoulder discomfort in the lower part of the exercise. Three participants (37.5%) used an incline bench of 20°-45° during the bench press to avoid lower back discomfort while laying

horizontally. In addition to avoiding low back discomfort, 1 participant (12.5%) also preferred an inclined bench press to prevent the feeling of choking while laying horizontally.

Feasibility of HLST Program

All 8 participants (100%) who completed baseline maximal strength testing attempted the HLST program. Details pertaining to the feasibility of the HLST exercise program are summarized in **Table 8.** Of the 8 participants who began the HLST program, the average attendance was 21.8 (90.6%) of the 24 supervised exercise sessions with a range from 17 to 24. Only 3 participants (37.5%) completed all 24 exercise sessions. The most common reasons for missed exercise sessions were: household chore/shoveling-related back strains, out of town for vacation or work, and death in the family. The mean duration of each exercise session was 60 minutes (95% CI: 55 to 66) and all 8 participants (100%) progressed to heavy loads (80-90% of 1RM) at session #9 or #10 (approximately 5-weeks). All 8 participants (100%) reached a peak volume of 5 sets and 6 repetitions at 90% 1RM in at least one of the main exercises (squat, bench press, and/or deadlift). Sets and reps were decreased for one participant's bench press due to feeling fatigued that day. For 1 participant (12.5%), we exceeded 90% of their predicted squat 1RM for 4 sessions, as they did not perform a true 3RM test at baseline. All 8 participants (100%) responded well to an increase in total volume (sets x reps x load) from session to session after heavy loads were reached. No exercise-related adverse events were observed or reported during the supervised HLST sessions.

Follow-up Assessment Rate

Six participants (75%) completed all follow-up maximal strength tests. One participant was cautious on all follow-up strength tests as they did not want to aggravate previous back muscle pain. Another participant could not complete the deadlift even at light loads (50% baseline 1RM) due to extreme stomach pain the previous night and day of testing. This pain was aggravated in the

bent over deadlift position. The total mean duration of the post-intervention physical assessment was 2.37 hours (95% CI: 1.77 to 2.97); an increase of 12.5 minutes from baseline testing duration. The duration of the post-intervention physical assessment increased from baseline for 5 participants (62.5%).

Seven participants (87.5%) completed the follow-up questionnaires in their entirety. One participant (12.5%) had extreme stomach pain the night before and day of testing. He confirmed that his responses to the postintervention questionnaires were based on how he was currently feeling, which was terrible. This may not be an accurate reflection of a typical day in his life. One other participant (12.5%) refused to answer questions about engaging in a HLST program over the next 6 months because she said she could not predict the future.

Effects of HLST on Health-Related Fitness and Patient-Reported Outcomes

Descriptive statistics for changes in health-related fitness outcomes are presented in **Table 9.** Changes in all primary outcomes were statistically significant for all strength exercises. Weight lifted from baseline to post HLST increased for the squat/leg press (median change: +36 kg; 95% CI: +25 to +47; p=0.012), bench press (median change: +7 kg; 95% CI: +2 to +10; p=0.012), and deadlift (median change: +13 kg; 95% CI: +6 to +25; p=0.018). In addition, the total weight of the 3 strength exercises combined significantly increased from baseline to post HLST (median change: +55 kg; 95% CI: +40 to +72; p=0.012). No significant changes were reported in secondary physical functioning outcomes, including active shoulder ranges of motion (flexion and abduction), 6MWT, and the 30 second sit to stand test.

Significant changes were reported in our tertiary physical health outcomes including resting systolic blood pressure (median change: -10.0 mmHg; CI: -17 to -6; p=0.012), resting diastolic blood pressure (median change: -13 mmHg; 95% CI: -16 to -4; p=0.017), and resting

heart rate (median change: -6 bpm; 95% CI: -10 to -1; p=0.035). No significant changes were reported in weight or waist to hip ratio.

Descriptive statistics for changes in health-related quality of life (EORTC QLQ-C30) are presented in **Table 10.** Overall, no significant changes were reported in functional or symptom scales. However, significant findings were reported for the global health status/quality of life measure (median change: +8.3; 95% CI: 0 to +16.7, p=0.041).

Descriptive statistics for changes in patient-reported symptoms and psychosocial outcomes are presented in **Table 11.** Overall, no significant changes were reported in patient-reported symptoms and psychosocial outcomes from baseline to post HLST.

Effects of HLST on Motivation, Benefits, and Barriers

Descriptive statistics for changes in motivational and behavioural outcomes are presented in **Table 12.** Overall, motivational and behavioural outcomes were high at baseline, and remained high post HLST, but no statistically significant changes were reported. However, the duration of weekly of aerobic exercise (median change: +150 mins; 95% CI: -128 to +527) and non-trial weight training (median change: +67 ins; 95% CI: -15 to +170) improved, but were also not statistically significant.

Descriptive statistics for changes in perceived benefits of HLST are presented in **Table 13.** All 8 participants (100%) believed that the HLST program was highly beneficial for their physical fitness and muscular strength. Seven participants (87.5%) reported better sense of control over health, less fatigue to carry out daily activities, and better overall quality of life after the HLST program**.** Five participants (62.5%) reported better ability to stop thinking about their cancer, better shoulder/neck pain or injury, and better shoulder/neck motion**.** Only 1 participant (12.5%)

reported worse shoulder neck pain or injury, worse shoulder/neck motion, and worse fear of cancer recurrence.

Descriptive statistics for changes in perceived barriers to HLST are presented in **Table 14.** No barrier severely interfered with their ability to participate in HLST according to the 8 participants (100%). From the 8 participants, 0 (0%) reported the following to be significant barriers to HLST: fear of recurrence, bad weather, medical appointments, feeling tired, lack of motivation, too busy, muscle/joint pain, feeling sick, commute, or exercise program being too hard. Two participants (25%) reported having HNC as a perceived barrier to HLST. One participant (12.5%) reported muscle/joint injury and another one (12.5%) reported shoulder/neck pain as a perceived barrier to HLST.

Descriptive statistics for participants' motivation to continue HLST after the LIFTING trial are presented in **Table 15.** Over the next six months, all 7 participants (100%) who provided their response thought that a HLST program would be beneficial to continue. These 7 participants (100%) also thought that the HLST program would be somewhat, quite a bit, or very much enjoyable, and would have the necessary support to continue HLST. Five participants felt very much (71.4%) motivated and 2 participants (28.5%) felt somewhat motivated to continue HLST over the next six months. Participants reported mixed levels of confidence ranging from not at all confident to very much confident to continue HLST postintervention. Four participants (57.1%) felt that HLST would be a little bit difficult to continue on their own. However, four participants (57.1%) also felt they would have control over HLST over the next six months. Five participants (62.5%) had a detailed plan in place to some degree, or had at least thought through this and discussed exercise moving forward with the trial coordinator.

Discussion

Overall, preliminary findings of the LIFTING trial suggest that a HLST program may be feasible and safe for HNCS at least 1-year post-ND. We recruited about 1 HNCS per month over an 8 month period, which was less than our goal of 15-20. We were also unable to track the eligibility and recruitment rates or the reasons for not participating. HNCS who did join the study were able to complete maximal strength testing without major difficulties or any adverse events. Moreover, they attended over 90% of the HLST sessions and were able to progress to full prescription (90% 1RM) over the 12-week period. Furthermore, the HLST program resulted in significant improvements in muscular strength, resting heart rate, resting blood pressure, and global health status/quality of life. Conversely, no significant changes were reported in patient-reported symptoms and psychosocial outcomes or physical functioning outcomes. Most HNCS were highly motivated to do the HLST program and remained highly motivated after the program.

Due to recruitment methods, we were unable to accurately report the recruitment and eligibility rates in our study. This is because many study participants knew of other potentially eligible participants, and passed along information by word of mouth. In addition, information about the LIFTING trial was passed along to other medical professionals and cancer clinics via word of mouth. Furthermore, the study coordinator could not recruit in-person at the clinic due to COVID-19 restrictions. Therefore, it was not possible to track exactly how many people were contacted and informed about the LIFTING trial. Of the 14 potentially eligible and interested HNCS referred to the study coordinator, 8 HNCS (57%) were eligible, interested, and completed the HLST program. This equates to 1 participant recruited per month. Based on previous resistance training feasibility studies in HNCS, this recruitment rate is slightly lower than 1.38 HNCS (71) and 2.5 HNCS (40) per month. Although our eligibility rate is unknown, the eligibility

rate for exercise trials in HNCS posttreatment have been reported as 29.9% (those that expressed interest, not who would have been eligible) for a 12-week, supervised strength training program post radiation and/chemotherapy (71) and an eligibility rate of 47.3% was reported for a 12-week, supervised PRET post-ND (19). The main reasons for ineligibility in our study were not meeting the shoulder flexion and abduction requirements, and unmanaged comorbid disease. In the future, HNC trials should recruit in person from multiple clinics and cancer centres, and also consider mailing letters to potentially eligible HNCS through a cancer registry.

The maximal testing rate at baseline was 100%, where all participants completed all muscular strength tests. However, modifications to the 1RM test were made for 2 participants. One participant was unwilling to continue increase the weight to find their 1RM for the squat, and stopped at a peak 3RM. Another participant was unwilling to continue finding their 1RM for the deadlift, and stopped at a true 2RM. It is important to note that neither of these participants stopped due to pain, injury, or discomfort, and strictly not being willing to lift more. Their predicted 1RM was calculated based on these values. As a whole, 1RM testing was feasible in the LIFTING trial. However, future trials that plan to utilize the 1RM test should consider evidence-based motivational strategies to encourage study participants to continue to approach their true 1RM. In addition, familiarization sessions prior to 1RM testing may be unnecessary. A systematic review suggested that the 1RM has good to excellent test-retest reliability regardless of resistance training experience, number of familiarization sessions, exercise selection, upper versus lower body assessment, sex and age of participants (79). In addition, for older adults (mean: 70.7 years), 1RM prediction equations underestimate the actual 1RM (73).

The HLST program adherence rate of 90.6% is promising and similar to that reported in other supervised strength training trials in HNCS posttreatment (19, 40, 71). Most frequently

reported barriers to exercise post-ND were having HNC, followed by shoulder/neck pain and muscle/joint injury. These barriers may somewhat overlap with those that have been previously reported, which included dry mouth or throat, fatigue, shortness of breath, muscle weakness, difficulty swallowing, and shoulder weakness/pain (72). Suggested modifications to future HLST in HNCS may include the following. Instead of HNCS performing the bench press on a flat bench, considering an incline bench press (30-45°) could be a good idea to reduce any lower back and swallowing discomfort when laying horizontally. Including a foam barbell pad for squats could also be great to reduce upper back discomfort during the exercise, and standardize the movement among all participants. No participants dropped out of the study.

Follow-up assessment rates for postintervention maximal strength testing and questionnaires were excellent (75% and 87.5% respectively). This is comparable, and even slightly higher, than previous literature in exercise oncology trials that utilized 1RM testing and questionnaires; 71% of HNCS completed questionnaires post PRET (45); 81% of breast cancer patients completed all data collection including 1RM testing and questionnaires (50). The main reasons for not effectively completing maximal strength testing postintervention were due extreme stomach pain in 1 participant, and not wanting to aggravate previous muscle back pain in another participant. The same 1 participant reported worse shoulder neck pain or injury, worse shoulder/neck motion, and worse fear of cancer recurrence post HLST, as they were experiencing back muscle soreness that was likely unrelated to the HLST program. The one reason for not completing questionnaires pertaining to engaging in a HLST over the next 6 months was that 1 participant could not predict the future. Future studies of HLST in HNCS may anticipate 10-20% loss-to-follow-up and adjust their sample size accordingly.

Our study suggested significant improvements in upper and lower body muscular strength (squat, bench press, and deadlift) post-surgical ND after a HLST program from a total combined weight of 180 kg pre-HLST to 240 kg post-HLST, a 33% improvement. The 1RM strength improvements post HLST in the LIFTING trial for squat/leg press, bench press, and deadlift were: 44.6%, 18.6%, and 16.7%, respectively. Although there is no literature that involves HNCS participating in a HLST using free weights, there are 3 studies that examine heavy resistance exercise using machines in cancer populations. The results in the LIFTING trial were superior for changes in squat/leg press strength, and inferior to previous chest press and leg curl data. Although, different exercise types and machines were used.

A randomized crossover trial involving low loads (60%-65% of 1RM), and 2 sets of 15-20 repetitions; in addition to heavy loads (85%-90% of 1RM), and 3 sets of 5-8 repetitions was conducted in 21 newly diagnosed breast cancer patients receiving adjuvant chemotherapy with a prior axillary lymph node dissection (50). The authors examined the impact of heavy load lifting on the lymphatic system. Percent changes in muscular strength were not reported (50).

Another study administered a heavy resistance training program was conducted in 55 newly diagnosed breast cancer patients scheduled for adjuvant therapy. Study participants took part in this heavy resistance training program 2 times per week for a total of 12-weeks, and engaged in 4 sets of 4 repetitions of leg press at 90% 1RM. The authors reported an increase in 1RM leg press of 20% postintervention in the exercise group compared to pretest 1RM scores (51).

The final study examined a 12-week PRET program in 37 prostate cancer survivors on androgen deprivation therapy. Study participants engaged in 3 sets of 8-15 repetitions of machine-based resistance exercises, 3 days per week. The authors reported a 61.9% increase in leg press

10RM, a 59.3% increase in chest press 10RM, and a 30.1% increase in leg curl 10RM (17). No exercise oncology trials have directly assessed barbell bench press or deadlift strength. However, it is not entirely valid to compare changes in a machine-based 1RM with changes in free weight 1RM. Free weight exercises are much more technical and physically demanding movements. In addition, ranges for sets and repetitions, as well as testing measures were not identical across all studies (E.g., 1RM versus 10RM).

Moreover, our study suggested significant improvements in global health status/quality of life median change from pre-HLST to post-HLST of +8.3 points. However, there were no statistically significant changes reported for functional or symptom scores from baseline to post HLST. This may be because participants reported an excellent quality of life at baseline, and levels remained high post HLST. Moreover, no significant changes were reported in patient-reported symptoms and psychosocial outcomes from baseline to post HLST. This may be because participants did not report severe levels of symptom burden at baseline, so there was not much room for improvement. In addition, it is crucial to note that psychosocial outcomes were assessed during a highly stressful time, the COVID-19 global pandemic. The Behavioural Medicine Laboratory was required to close for all research activities from December 14, 2020 to January 24, 2021, and frequent uncertainties around remaining open afterwards remained. Therefore, results of specific items such as fatigue, anxiety, and insomnia may not be reflective of typical levels reported pre- and post-pandemic times. Overall, our data suggest that we recruited HNCS who were functioning quite well before the intervention.

In addition, our study also suggested significant changes in resting heart rate and blood pressure. The American Heart Association defines clinically significant blood pressure reduction as SBP reductions of ≥10 mmHg, or DBP reductions of ≥5 mmHg (72). Previous cardiac research

has suggested that changes in resting heart rate of >5 bpm are considered clinically meaningful (71). Therefore, the results of the LIFTING trial demonstrated that the reductions in resting heart rate and resting blood pressure were statistically and clinically significant.

Participants in the LIFTING trial reported high levels of motivational and behavioural outcomes at baseline, which remained high postintervention. Weekly exercise duration increased for both aerobic and non-trial weight training exercise from baseline to post HLST. However, no significant changes were reported for motivational or behavioural outcomes.

All participants in the LIFTING trial reported that the HLST program was beneficial in improving physical fitness and muscular strength. The majority reported that the HLST program was beneficial in improving sense of control over health, fatigue to perform daily activities, overall quality of life, ability to stop thinking about cancer, shoulder/neck pain or injury, and shoulder/neck motion. One participant reported worse shoulder/neck pain or injury, shoulder/neck motion, and fear of cancer recurrence post HLST. This participant had a back muscle strain that flared up a couple of times during the duration of the study. It was determined that the initial setback was unrelated to the exercise intervention and a result of house chores. The study coordinator and participant were both unsure about the cause of the second setback and whether or not the HLST may have contributed to this discomfort.

Our study suggested that participants did not experience significant barriers which would have impacted their ability participate in the HLST program. The most frequently reported barriers that somewhat made it difficult to participate in the HLST program post-ND were having head and neck cancer, followed by shoulder/neck pain and muscle/joint injury. These barriers may somewhat overlap with those that have been previously reported, which included dry mouth or throat, fatigue, shortness of breath, muscle weakness, difficulty swallowing, and shoulder

weakness/pain (72). However, the participant who reported shoulder/neck pain and muscle/joint injury was the same person.

Additionally, over the next six months, all study participants who provided their response thought that a HLST program would be beneficial to continue. The majority of participants felt very much motivated and in control, but the majority also reported that the HLST program would be a little bit difficult to continue. Mixed levels of motivation were reported for enjoyment, support, confidence, and having a detailed plan in place. These results suggest that HNCS may benefit from more independence (less supervision) at some point in order to feel completely confident in participating in a HLST program on their own. In addition, three participants were interested in continuing some kind of exercise on their own. These individuals were in touch with the study coordinator for guidance and to discuss exercise options that could be done at home. Furthermore, future studies may consider specifically educating study participants on exercise prescription to get them thinking through how to go about designing an exercise program for themselves when the intervention comes to an end, so that this task becomes less intimidating than it may sound initially.

Our study had important strengths and limitations. To our knowledge, the LIFTING trial is the first study to test the feasibility and safety of a HLST program in HNCS post-surgical ND. Moreover, the HLST program was supervised, and individualized to the needs and abilities of each participant. In addition, we carefully monitored and documented exercise modifications, reasons for missed sessions, and adverse events. Finally, we used validated measures to assess health-related fitness and patient-reported outcomes. Some limitations of our study include the failure to track eligibility and recruitment rates, the small sample size, non-randomized controlled design, lack of a comparison group, and no long-term follow-up. Nevertheless, since the LIFTING trial is

the first study to test a HLST program in HNCS post surgery, it was crucial to conduct a phase I study to determine the feasibility and safety of HLST before initiating larger randomized controlled trials.

In conclusion, the phase I LIFTING trial suggests that a supervised HLST program in HNCS ≥1-year post-ND is safe, feasible, and well-received by participants. Although there were challenges with recruitment, the study demonstrated excellent testing feasibility, adherence, follow-up rates, strength gains, and improvements in global health status/quality of life ≥1-year post-ND in those who did participate. Whenever possible, in-person recruitment across multiple HNC clinics would be ideal. Phase II trials are warranted to establish the risks and benefits of HLST in HNCS.

TABLES

Table 1. Repetition Maximum and Rest Period Continuum for Resistance Training

Primary Parameter	**Load**	**Reps**	**Sets**	**Rest Between Sets (minutes (m))**
Strength	80-90% 1RM	1-6	3-5	3-5 m
Hypertrophy	70-75% 1RM	6-12	3-4	1-2 m
Endurance	50-65%	12-30	3-6	0.33-1m

Table 2. 12 Week HLST Exercise Program Intensities for Main Movements

Week/Session	Movements	Sets x Reps @ %/RPE
1/Day 1	Back Squat + Bench Press	2 x 10 @ 50%/RPE 5
1/Day 2	Deadlift + Back Squat	
2/Day 3	Back Squat + Bench Press	3 x 8 @ 60%/RPE 6
2/Day 4	Deadlift + Back Squat	
3/Day 5	Back Squat + Bench Press	2 x 6 @ 65%/RPE 6 + 2 x 5 @ 70%/ RPE 7
3/Day 6	Deadlift + Back Squat	
4/Day 7	Back Squat + Bench Press	2 x 6 @ 70%/RPE 7 + 2 x 5 @ 75%/RPE 7
4/Day 8	Deadlift + Back Squat	
5/Day 9	Back Squat + Bench Press	3 x 6 @ 75%/RPE 7 + 2 x 2 @ 80%/RPE 8
5/Day 10	Deadlift + Back Squat	
6/Day 11	Back Squat + Bench Press	3 x 3 @ 80%/RPE 8 + 2 x 2 @ 85%/RPE 8
6/Day 12	Deadlift + Back Squat	
7/Day 13	Back Squat + Bench Press	3 x 3 @ 85%/RPE 8 + 2 x 1 @ 90%/RPE 9
7/Day 14	Deadlift + Back Squat	
8/Day 15	Back Squat + Bench Press	4 x 3 @ 80%/RPE 8
8/Day 16	Deadlift + Back Squat	
9/Day 17	Back Squat + Bench Press	3 x 1 @ 90%/RPE 9 + 2 x 3 @ 80%/RPE 8
9/Day 18	Deadlift + Back Squat	
10/Day 19	Back Squat + Bench Press	3 x 2 @ 85%/RPE 8 + 2 x 4 @ 80%/RPE 8
10/Day 20	Deadlift + Back Squat	
11/Day 21	Back Squat + Bench Press	3 x 2 @ 90%/RPE 9 +
11/Day 22	Deadlift + Back Squat	

		2 x 3 @ 80%/RPE 8
12/Day 23	Back Squat + Bench Press	3 x 1 @ 90%/RPE 9 + 3 x 2 @ 80%/RPE 8
12/Day 24	Deadlift + Back Squat	

Table 3. 12 Week Exercise Program Intensities for Accessory Movements

Week/Session	Movements	Sets x Time (seconds (s)) or Reps/RPE
1/Day 1	Dumbbell Farmers Carry + Front and Side Planks	2 x 15s/RPE 5
1/Day 2	Bodyweight Lunges + Face Pulls + Pushups (modify as needed)	2 x 14/RPE 5
2/Day 3	Dumbbell Farmers Carry + Front and Side Planks	3 x 15s/RPE 6
2/Day 4	Dumbbell Lunges + Face Pulls + Pushups (modify as needed)	3 x 14/RPE 6
3/Day 5	Dumbbell Farmers Carry + Front and Side Planks	3 x 20s/RPE 6
3/Day 6	Dumbbell Lunges + Face Pulls + Pushups (modify as needed)	3 x 12/RPE 6
4/Day 7	Dumbbell Farmers Carry + Front and Side Planks	3 x 25s/RPE 7
4/Day 8	Dumbbell Lunges + Face Pulls + Pushups (modify as needed)	3 x 10/RPE 7

5/Day 9	Dumbbell Farmers Carry + Front and Side Planks	3 x 30s/RPE 7
5/Day 10	Dumbbell Lunges + Face Pulls + Pushups (modify as needed)	3 x 10/RPE 7
6/Day 11	Dumbbell Farmers Carry + Front and Side Planks	3 x 30s/RPE 8
6/Day 12	Dumbbell Lunges + Face Pulls + Pushups (modify as needed)	3 x 12/RPE 8
7/Day 13	Dumbbell Farmers Carry + Front and Side Planks	4 x 25s/RPE 8
7/Day 14	Dumbbell Lunges + Face Pulls + Pushups (modify as needed)	4 x 12/RPE 8
8/Day 15	Dumbbell Farmers Carry + Front and Side Planks	4 x 35s/RPE 9
8/Day 16	Dumbbell Lunges + Face Pulls + Pushups (modify as needed)	4 x 14/RPE 9

9/Day 17	Dumbbell Farmers Carry + Front and Side Planks	3 x 40s/RPE 8
9/Day 18	Dumbbell Lunges + Face Pulls + Pushups (modify as needed)	3 x 16/RPE 8
10/Day 19	Dumbbell Farmers Carry + Front and Side Planks	3 x 40s/RPE 9
10/Day 20	Dumbbell Lunges + Face Pulls + Pushups (modify as needed)	3 x 14/RPE 9
11/Day 21	Dumbbell Farmers Carry + Front and Side Planks	3 x 45s/RPE 8
11/Day 22	Dumbbell Lunges + Face Pulls + Pushups (modify as needed)	3 x 16/RPE 8
12/Day 23	Dumbbell Farmers Carry + Front and Side Planks	4 x 45s/RPE 8
12/Day 24	Dumbbell Lunges + Face Pulls + Pushups (modify as needed)	4 x 16/RPE 8

Table 4. HLST in Cancer Populations

Author	Sample	Study Design	Intervention	Outcome/Measures	Findings	Limitations
Bloomquist et al., 2018	**n=21** women receiving standard adjuvant chemo for stage I-III breast cancer who had an axillary lymph node dissection.	Randomized, crossover equivalence trial	**Low-load**: 60%–65% 1RM, 2 sets of 15–20 reps of upper extremity resistance exercise. **Heavy-load**: 85%–90% 1RM, 3 sets of 5–8 reps of upper-extremity resistance exercise. Assessed before, after, 24 and 72 hours post exercise, and a 7 day washout period between	**Primary:** extracellular fluid. **Secondary:** interarm volume percent difference and subjective assessment of breast cancer-related arm lymphedema symptoms.	Similar lymphatic response with low- and high-loads. Less swelling at 72 hours post exercise with heavy-loads.	Activities engaged within the 3 days after low- or high-load resistance training may have influenced data collected at 24 or 72 hours post exercise.
Cešeiko et al., 2019	**n=55** women newly diagnosed with stage I-III breast cancer scheduled for adjuvant therapy.	Randomized controlled trial	**Maximal strength testing (MST):** 4x4 reps of dynamic leg press at ~90% 1RM twice a week for 12-weeks. **Control group:** instructed to perform 3 sets of 10 chair rises twice a week for 12 weeks.	Dynamic maximal strength of lower extremities, walking economy, time to exhaustion, quadriceps femoris muscle mass, and functional performance.	Improvements in lower extremity muscle strength, walking economy, functional performance, overall quality of life, and maintained muscle mass. Completion rate: 96% with no injuries reported, suggesting MST using the leg press machine to be a feasible and safe exercise modality for this population.	Only one exercise performed (leg press) and no upper body exercises prescribed. Disconnect between measure of assessment used (30 second sit to stand test) and the goal of the MST protocol (increase maximal muscle strength, muscle mass, walking economy, and functional performance). Lack of measurements of neural and muscular components.

Dawson et al., 2018	**n=37** prostate cancer patients on androgen deprivation therapy	Pilot randomized controlled trial **Exercise Groups:** Resistance training and protein supplementation (50g/day whey protein isolate) (TRAINPRO); Resistance training (TRAIN) **Non-Exercise Groups:** Protein Supplementation (50g/day whey protein isolate) (PRO); Control Stretching (STRETCH)	12-weeks, 3 days per week of PRET **Type:** 7 machine-based (leg press, leg curl, leg extension, chest press, shoulder press, seated row, lat pulldown); 3 trunk exercises (plank, hip bridge, deadbug) at percentage of 10RM. **Weeks 1–2:** 60% 1RM, 15 reps **Weeks 3–4:** 65–67%, 15–12 reps **Weeks 5–6:** 70% 1RM, 12–10 reps **Weeks 7–8:** 75% 1RM, 10–8 reps **Weeks 9–10:** 80% 1RM, 10–8 reps **Weeks 11–12:** 83% 1RM, 8 reps	Body composition, metabolic syndrome, quality of life, physical fitness, and muscular strength.	Improvements in sarcopenia, body fat percentage, strength, and quality of life. No changes in metabolic syndrome or physical function. Protein supplementation (50g/day of whey protein isolate) provided no additional benefit in improving body composition.	Non-sedentary control group with level of physical activity at baseline. Self-reported physical activity. Supervised exercise limits the generalizability of results to home- or group-based settings. Lack of racial variability (50% white) limits the generalizability to minority groups.

Table 5. Exercise Interventions in HNC Populations

Author	Sample	Study Design	Intervention	Outcomes	Findings
Capozzi et al., 2015	**n=21** stages I-IV (or unknown stage) HNCS both on and completed radiation or concurrent chemo-radiation treatment	RCT	12-weeks, 3 days per week of PRET. **Sets:** 2; **Reps:** 8-10; **Type:** 10 full body	**Primary:** feasibility (recruitment, adherence, and safety) **Secondary:** health-related fitness (anthropometrics, hand grip strength, functional performance, and cardiorespiratory fitness) and symptom management (pain, tiredness, nausea, depression, anxiety, drowsiness, appetite, overall wellbeing, and shortness of breath	Progressive strength training for HNCS is feasible. Significant improvements in fitness and physical functioning outcomes. Statistically and clinically significant acute symptom management improvements for tiredness and drowsiness.
Lonbro et al., 2013.	**n=30** HNSCC of the larynx (except glottic stage I II), pharynx, oral cavity or in lymph nodes from an unknown primary tumor, stage I – IV, and tumor node metastasis classificatio n.	Randomized stratified and parallel-grouped feasibility study	12-week PRET, 2-3 sessions for the first 2-weeks and an average of 5 sessions over the past 10-weeks. **Sets:** 2; work up to 2 sets; **Reps:** 12; work up to 8 RM; **Type:** 7 full body **Protein Creatine (PROCR) Group:** 7 day pre-trial creatine loading protocol followed by 12-weeks of PRET protocol with creatine and protein supplementation **Placebo (PLA) Group:** 7 day pre-trial placebo ingestion followed by the same PRET protocol with placebo supplementation.	**Primary:** feasibility **Secondary:** examine group changes over time and group difference of lean body mass, muscle strength, and functional performance	PRET showed to be safe and feasible in HNSCC patients, with a high adherence (97%) and completion rate (70%). No significant differences between groups. Significant increases in lean body mass, strength, and functional performance in both groups.
Lonkvist et al., 2017	**n=12** HNSCC (pri mary tumor in the nasal cavity, oral cavity, pharynx, or larynx), stage III or IV, and receiving concomitant chemoradiot herapy.	Prospective pilot study	12-weeks of PRET, 3 days weekly. **Sets:** progress from 2 to 3; **Reps:** progress from 15 to 8 (heavier); **Type:** 7 large exercises involving large muscle groups (abdominal crunches, back extensions, chest press, low row, hamstring curls, knee	**Primary:** feasibility (attendance to training sessions) **Secondary:** changes in functional performance, muscle strength, body composition, adverse events, dietary intake, self-reported physical activity, and quality of life	PRET is safe in feasible in HNC patients undergoing concomitant chemo-radiotherapy. High patient satisfaction (social and psychological benefits) and adherence rate (93%). Functional performance was maintained during treatment and increased during the 13 months follow up visit. No

			extensions, and leg press).		adverse events related to PRET.
McGarvey et al., 2013	**n=10** surgical ND (uni- or bilateral) for HNC, presenting with shoulder pain and spinal accessory nerve injury on the operated side. 80% males; 20% females.	Comparative Design	7 dynamic strengthening exercises with a 2.0kg weight, with attention given to scapular form. 3 second concentric and eccentric phases, 30 and 60 second rest between reps and exercises respectively. **Sets:** 1; **Reps:** 3; **Type:** shoulder shrug, overhead press, row standing, row prone, adduction/flexion, wall press-up, and protraction supine	**Primary:** to investigate which exercises had the highest dynamic surface electromyographic activity (SEMG) of the trapezius muscle post ND **Secondary:** Assess potential differences in muscle activity between the affected and unaffected side post surgery	SEMG was lower in the affected side compared to the unaffected side. Affected side showed higher levels of upper and middle trapezius muscle activity during overhead movements. Affected side had higher muscle activity in the rhomboid and serratus anterior compared to the unaffected side. Rhomboid and serratus anterior compensate for the muscular deficits in the upper and middle trapezius.
McNeely et al., 2004	**n=20** HNSCC managed by definitive surgical resection	Pilot study of a randomized controlled design	**Exercise Group: n=10** 12-week supervised PRET, 3 times weekly. **Sets:** progress from 1 to 2; **Reps:** progress from 15 to 20; **Type:** 6 therapeutic exercises (scapular retraction, scapular elevation, elbow flexion, elbow extension, external rotation, and abduction in the plane of the scapula) **Control Group: n=10** active and passive range of motion exercises and stretching exercises with a resistance band but no PRET	**Primary:** recruitment rate, completion rate, and adherence rate **Secondary:** shoulder function, shoulder pain and disability, and quality of life	High completion rate (85%) and adherence rate (93%). Resistance training may be used alongside standard physical therapy protocols in post-surgical HNC patients.
McNeely et al., 2004	**n=3** case reports HNC patients managed by radical ND	Case report	**PRET Group n=3:** 2-3 days weekly **Sets:** progress from 1 to 2; **Reps:** progress from 25 to 12-15; **Type:** seated or prone row, shoulder shrug, elbow flexion, elbow extension, resisted external rotation, and	**Primary:** to demonstrate the beneficial role of PRET in improving shoulder pain and dysfunction for HNC patients	Shoulder pain may be enhanced by inappropriate exercise prescription, poor exercise performance, or both. Specific exercises are required to maintain stabilization and obtain adequate muscle action.

			abduction in place on scapula		Beneficial effect on pain. Ongoing functional deficits were still present in all patients. Less than optimal functional improvement.
McNeely et al., 2008	**n=52** HNCS; cancer managed by definitive surgical resection	Prospective, randomized controlled trial	**PRET Group n=27:** 12-week supervised, active and passive range of motion/stretching, postural exercises, and basic strengthening exercises with light weights (1–5 kg) and elastic resistance bands **Sets:** 2; **Reps:** 10 to 15 at 25%-30% 1RM, and progress to 60%-70% of 1RM; **Type:** 5 to 8 upper body exercises **Standardized Therapeutic Exercise Protocol (TP) Group: n=25** same active and passive range of motion/ stretching and postural exercises as the PRET group Both groups focused on the rhomboids/middle trapezius, levator scapula/upper trapezius, biceps, triceps, deltoid, and pectoralis major muscles	**Primary:** change in patient-rated shoulder pain and disability from baseline to post-intervention **Secondary:** endpoints were upper extremity strength and endurance, range of motion, fatigue, and quality of life	High rate of follow-up assessment (85%) and excellent adherence to the PRET program (93%). PRET significantly reduced shoulder pain and disability, and improved upper extremity muscular strength and endurance in HNCS who had shoulder dysfunction due to spinal accessory nerve damage post resection.
McNeely et al., 2015	**n=52** HNCS; cancer managed by definitive surgical resection	12-month follow-up data from randomized crossover trial comparing PRET with a standard therapeutic protocol (TP) in post-surgi-cal HNC survivors.	**PRET Group: n=27** same as above **Sets:** 2; **Reps:** 10 to 15 at 25%-30% 1RM and progress to 60%-70% of 1RM; **Type:** 5 to 8 upper body exercises **TP Group: n=25** same as above	**Primary:** patient-reported shoulder pain and disability, sustainability in the long term **Secondary:** ND impairment, fatigue, and quality of life	44 of 52 patients eligible at 12 month follow up. Self-reported outcomes of the benefits of PRET were largely sustained at the follow up period. Participants who continued resistance exercise training regardless of group assignment reported better ND-related functioning and better quality of life

			Both groups focused on the rhomboids/middle trapezius, levator scapula/upper trapezius, biceps, triceps, deltoid, and pectoralis major muscles		than patients who did not.
Rogers et al., 2013	**n=15** HNC patients receiving radiation therapy	Pilot, 2-arm, randomized controlled trial	**Intervention Group n=7:** resistance exercise with nutrition counselling. 12-week resistance program, 2 times weekly, with supervised sessions for the first 6-weeks. 2 home-based sessions weekly with telephone counselling, written materials, and DVD after the 6-week supervision phase. **Reps:** up to 10; **Type:** 9 exercises using resistance bands or weight machines (chest press, leg extension, lateral row, reverse curl, tricep wall pushup or tricep kickbacks, heel raise, front shoulder raise, hamstring curl, and arm curl) **Control Group n=8:** nutrition counselling alone from a registered dietician. No specific recommendations were given regarding engaging or not engaging in aerobic or resistance training.	**Primary:** feasibility (eligibility rates, recruitment rates, retention rates, adverse events, intervention process evaluation, and exercise adherence). **Secondary:** intervention effects on muscle strength, lean body mass, physical functioning, fatigue, and quality of life.	No serious adverse events occurred that were related to the exercise intervention. Significant improvements in perceived fatigue and quality of life at 6-weeks in the exercise group compared to the control group, and improvements in chair rise time at 6 and 12-weeks for the exercise group. Resistance exercise training has been demonstrated to be safe and feasible for HNC patients undergoing radiation therapy.
Samuel et al., 2013	**n=48** HNC patients undergoing chemoradiotherapy (CRT)	RCT	**Exercise Group n=24:** 6-week individualized, active resisted exercise program and aerobic program **Aerobic:** brisk walking, 5 days per week for 15-20 minutes, at an RPE pf 3-5/10.	**Primary:** functional capacity and QoL	No adverse events or protocol deviations reported that were related to the exercise intervention. Significant differences for 6MWT for both groups. Distance increased in exercise group (improved functional capacity), and decreased in control group

			Active Exercise: seated exercises for upper and lower limbs (biceps, triceps, hamstrings, and quadriceps) 5 days per week. 3-5 sets of 8-10 reps. **Control Group n=24:** standard hospital care. Did not receive any specific exercises, but were advised to remain as active as possible during the study period.		(decreased functional capacity). Physical component score remained almost the same in the exercise group, and the mental component score increased significantly. Both physical and mental QoL scores decreased in the control group. Significant decrease (75.21%) in mental component score. A walking and active exercise program is safe and well-tolerated by HNC patients undergoing CRT.

Table 6. Baseline Demographic and Health Characteristics of Participants in the LIFTING Trial

Demographic	**Mean**	**SD**
Age (years)	65.63	7.05
Weight (kg)	81.79	8.46
Body Mass Index (kg/m^2)	25.61	0.94
Time Since Surgery (years)	7.5	4.69
	N (%)	
Sex		
Male	7 (87.5%)	
Female	1 (12.5%)	
Body Mass Index (kg/m2)		
≤25	2 (25%)	
>25 to <30	6 (75%)	
≥30.0	0 (0%)	
Marital Status		
Married	5 (62.5%)	
Common Law		
Divorced/Separated	2 (25%)	
Widowed		
Never Married	1 12.5%)	
Education		
<College/University		
≥College/University	8 (100%)	
Annual Family Income ($)		
<20,000	1 (12.5%)	
20,000-39,000	1 (12.5%)	
40,000-59,000	1 (12.5%)	
60,000-79,000	1 (12.5%)	
80,000-99,000		
>100,000	3 (37.5%)	
Prefer Not to Answer	1 (12.5%)	
Employment Status		
Employed Full- or Part-Time	3 (37.5%)	
Homemaker		
Disability or Sick Leave	1 (12.5%)	
Temporarily Unemployed		
Retired	4 (50%)	
Ethnicity		
Aboriginal		
African		
American		
Asian		
Caribbean		
White	8 (100%)	
Latin/Central/South America		
Middle Eastern		
Pacific Islander		
Behavioural		
Smoking Status		
Ex-Smoker	3 (37.5%)	
Current Smoker	1 (12.5%)	
Never Smoked	4 (50%)	
Drinking Status		

Ex-Drinker	3 (37.5%)
Current Drinker	4 (50%)
Never Drank	1 (12.5%)
Exercise Status	
Current Aerobic Exerciser Only	4 (50%)
Current Resistance Exerciser Only	
Current Aerobic + Resistance Exerciser	3 (37.5%)
Current Non-Exerciser	1 (12.5%)
Medical	
Cancer Type	
Tongue/Base of Tongue	5 (62.5%)
Oropharynx	1 (12.5%)
Larynx	1 (12.5%)
Unknown primary	1 (12.5%)
Cancer Stage	
TxN2a	1 (12.5%)
TxN2c	1 (12.5%)
T1N2	1 (12.5%)
T2N1	1 (12.5%)
T2N2b	1 (12.5%)
T2N2bMx	1 (12.5%)
T3N2c	1 (12.5%)
T4aN2C	1 (12.5%)
HPV Status	
Positive	5 (62.5%)
Negative	1 (12.5%)
Unknown	2 (25%)
Neck Dissection	
Unilateral	0 (0%)
Bilateral	7 (87.5%)
Unknown	1 (12.5%)
Time Since Surgery	
<5 years	2 (25%)
≥5 years	6 (75%)
Chemotherapy	
Yes	4 (50%)
No	4 (50%)
Radiation	
Yes	8 (100%)
No	0 (0%)
Biological/Hormone/Targeted Therapy	
Yes	1 (12.5%)
No	7 (87.5%)
Formal Rehabilitation Program	
Yes	8 (100%)
No	0 (0%)

Table 7. Feasibility of Baseline Maximal Strength Testing in the LIFTING Trial

Subject ID	Issues/Challenges	Results/Modifications	Performed All Fitness Tests (Y/N)	Duration of Assessment (mins)
LIFT 01	None	**Squat:** Completed successfully; no modifications **Bench Press:** Completed successfully; no modifications **Deadlift:** Completed successfully; no modifications	Y	150
LIFT 02	None	**Squat:** Completed successfully; no modifications **Bench Press:** Completed successfully; no modifications **Deadlift:** Completed successfully; no modifications	Y	120
LIFT 03	Yes. Squat with towel for comfort.	**Squat:** Completed successfully, but with modification. Towel on upper back for comfort. Completed 3RM. Peak max, not true maximal test base don observation. Unwilling to do more. 1RM calculation was applied for exercise prescription. **Bench Press:** Completed successfully; no modifications **Deadlift:** Completed successfully; no modifications	Y	120
LIFT 04	Yes. Skin graft (thigh as donor site), tongue reconstruction, discomfort laying horizontally for bench press.	**Squat:** Leg press used instead of barbell back squat due to instability and discomfort in lower body. Possibly due to less muscle mass/strength in left thigh as a result of nerve/skin grafts in attempt to reconstruct tongue. **Bench Press:** Incline bench notch #3 (30°-45°) due to discomfort on lower back and feeling of choking when laying flat. **Deadlift:** Completed 2RM. Unwilling to do more. 1RM calculation was applied for exercise prescription.	Y	105
LIFT 05	None. Squat with towel for comfort, restricted shoulder external rotation for bench press.	**Squat:** Completed successfully with modification. Towel on upper back for comfort. **Bench Press:** Completed successfully with modification. Lower barbell 1-2 inches above sternum. **Deadlift:** Completed successfully; no modifications	Y	140
LIFT 06	None. Squat with towel for comfort, bench press felt better on shoulder when not touching chest for bench press.	**Squat:** Completed successfully with modification. Towel on upper back for comfort. **Bench Press:** Lower barbell 1-2 inches above sternum **Deadlift:** Completed successfully; no modifications	Y	135
LIFT 07	Yes. Discomfort laying horizontally for bench press.	**Squat:** Completed successfully; no modifications **Bench Press:** Completed successfully with modification. Incline bench to notch #2 (20°-30°) due to discomfort on lower back when laying flat as a result of previous back surgery. **Deadlift:** Completed successfully; no modifications	Y	140
LIFT 08	Yes. Prior shoulder injury, discomfort laying horizontally for bench press.	**Squat:** Completed successfully with modification. Leg press used instead of barbell back squat due to bar sitting too high on cervical spine. Inability to lower bar to trapezius. Possibly due to prior rotator cuff injury and shoulder deterioration with age. **Bench Press:** Incline bench to notch #3 (30°-45°) due to discomfort on lower back. **Deadlift:** Completed successfully; no modifications	Y	135

Table 8. Feasibility of Heavy LIFTING Strength Training in the LIFTING Trial

Study ID	Attendance N (%)	Number of Weeks to Complete Sessions	Reasons for Non-Adherence	Average Time Per Session (minutes)		Ability to Reach Heavy Loads (Y/N)	Progression Timepoint (session #)	Peak Volume Achieved for ≥1 Exercises	Adverse Events	Exercise-Related (Y/N/U)
				Mean (SD)	Range					
LIFT 01	23/24 (95.8%)	12 weeks 6.5 week break after session #4 due to COVID-19 restrictions	Strained back when shovelling snow. Injury not related to the trial intervention. Delayed session #15 to be on the safe side and not aggravate injury.	75 (13.49)	38-92	Y	Session #10	Squat Sets: 5 Reps: 6 %Max:90	Strained low back.	N
LIFT 02	24/24 (100%)	12 weeks	N/A	62 (10.29)	42-79	Y	Session #10	Squat Sets: 5 Reps: 6 %Max:90	None	N/A
LIFT 03	17/24 (70.8%)	15 weeks	Delayed session #6 and 7 due to strained back muscle during outdoor house chores. Not trial-related. June 8-20 off to rest back; delayed sessions #18-21. Unsure if trial-related. Missed session #24 to complete final assessment before 2 week vacation.	59 (12.07)	34-86	Y	Session #9	Bench Press Sets: 5 Reps: 6 %Max:90	Tight back muscle.	N/U
LIFT 04	24/24 (100%)	12 weeks	N/A	59 (7.35)	52-68	Y	Session #9	Leg Press & Bench Press Sets: 5 Reps: 6 %Max:90	None	N/A

LIFT 05	23/24 (95.8%)	12 weeks	Out of town for work.	60 (9.19)	40-76	Y	Session #10	Squat & Bench Press Sets: 5 Reps: 6 %Max:90	None	N/A
LIFT 06	18/24 (75%)	15 weeks	Sick for session #5. Delayed to ensure no lingering symptoms. Delayed sessions #12, 13, and 14; out of town. Delayed session #17; not feeling well from wildfire smoke. Delayed session #19; car in shop.	56 (7.31)	46-70	Y	Session #10	Squat & Deadlift Sets: 5 Reps: %Max:90	None	N/A
LIFT 07	21/24 (87.5%)	10 weeks	Did not complete sessions #22, 23, and 24 because of death of father. Had to travel to England for 1 month. Final assessment before he left.	54 (10.62)	32-74	Y	Session #10	Squat Sets: 5 Reps: 6 %Max:90	None	N/A
LIFT 08	24/24 (100%)	12 weeks	N/A	57 (9.11)	38-72	Y	Session #10	Leg Press & Deadlift Sets: 5 Reps: 6 %Max:90	None	N/A

Table 9. Changes in Health-Related Fitness Outcomes from Baseline to Postintervention in the LIFTING Trial

Outcomes	Baseline Median (IQR)	Postintervention Median (IQR)	Median Change (95% CI)	p value
Primary Outcomes (kg)				
Squat/Leg Press (n=8)	83 (66 to 106)	120 (93 to 155)	+36 (+25 to +47)	0.012
Bench Press (n=8)	43 (37 to 51)	51 (40 to 59)	+7 (+2 to +10)	0.012
Deadlift (n=7)	66 (57 to 84)	77 (68 to 114)	+13 (+6 to +25)	0.018
Total (n=7)	180 (167 to 222)	240 (200 to 282)	+55 (+40 to +72)	0.012
Secondary Outcomes (n=8)	**Baseline Median (IQR)**	**Postintervention Median (IQR)**	**Median Change (95% CI)**	**p value**
Active Right Shoulder Flexion (°)	162° (154 to 170)	163° (155 to 170)	+2 (-13 to +18)	0.77
Active Right Shoulder Abduction (°)	161° (147 to 168)	164° (157 to 169)	+3 (-4 to +15)	0.46
Active Left Shoulder Flexion (°)	164° (152 to 170)	166° (153 to 174)	-1 (-13 to +16)	1.00
Active Left Shoulder Abduction (°)	165° (159 to 169)	163° (159 to 164)	-2 (-8 to +5)	0.46
6 Minute Walk Test (m)	578 (520 to 623)	597 (524 to 656)	+16 (-21 to +48)	0.32
30 Second Sit-to-Stand (#)	19 (17 to 27)	19 (15 to 26)	0 (-2 to +1)	0.71
Tertiary Outcomes (n=8)	**Baseline Median (IQR)**	**Postintervention Median (IQR)**	**Median Change (95% CI)**	**p value**
Weight (kg)	80 (76 to 83)	79 (74 to 83)	-0.9 (-3 to +1)	0.32
Resting Heart Rate (bpm)	72 (67 to 76)	66 (61 to 72)	-6 (-10 to -1)	0.035
Systolic Blood Pressure (mmHg)	128 (119 to 132)	116 (108 to 122)	-10 (-17 to -6)	0.012
Diastolic Blood Pressure (mmHg)	78 (71 to 82)	62 (61 to 70)	-13 (-16 to -4)	0.017
Waist to Hip Ratio	0.93 (0.90 to 1.03)	0.95 (0.90 to 1.0)	+0.01 (-0.04 to +0.05)	0.79

IQR=interquartile range, 25th and 75th percentiles

Table 10. Changes in EORTC QLQ-C30 from Baseline to Postintervention in the LIFTING Trial

EORTC QLQ-C30	Baseline	Postintervention	Median Change (95% CI)	p value
	Median (IQR)	Median (IQR)		
Overall score				
Functional Scales(n=8)				
Physical Functioning	100 (95.0 to 100)	100 (100 to 100)	0 (-3.3 to +3.3)	0.56
Role Functioning	100 (100 to 100)	100 (87.5 to 100)	0 (-8.3 to +8.3)	0.56
Emotional Functioning	91.7 (77.1 to 100)	100 (75.0 to 100)	0 (-8.3 to +12.5)	0.41
Cognitive Functioning	83.3 (71.0 to 97.0)	83.3 (71.0 to 100)	0 (-8.3 to +16.7)	1.00
Social Functioning	94.1 (71.0 to 100)	95.3 (71.0 to 100)	0 (-8.3 to +1.2)	0.65
Symptom Scales (n=8)				
Fatigue	11.0 (0 to 30.5)	0 (0 to 33.3)	0 (-5.5 to +5.7)	1.00
Nausea and Vomiting	0 (0 to 0)	0 (0 to 0)	0 (0 to +8.3)	0.31
Pain	0 (0 to 16.7)	0 (0 to 12.5)	0 (-8.3 to +8.3)	0.56
Dyspnea	0 (0 to 25.0)	0 (0 to 0)	0 (-16.7 to 0)	0.31
Insomnia	16.7 (0 to 33.3)	0 (0 to 33.3)	0 (-16.7 to 0)	0.31
Appetite Loss	0 (0 to 0)	0 (0 to 0)	0 (-16.7 to +16.7)	1.00
Constipation	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	1.00
Diarrhea	0 (0 to 0)	0 (0 to 0)	0 (0 to +16.7)	0.31
Financial Difficulties	0 (0 to 3.5)	0 (0 to 25.0)	0 (0 to +14.3)	0.31
Global Health Status/QoL (n=8)				
Global Health Status/Quality of Life	79.2 (66.7 to 96.0)	87.5 (83.3 to 98.0)	+8.3 (0 to +16.7)	0.041

IQR=interquartile range, 25th and 75th percentiles

Table 11. Changes in Patient-Reported Symptom and Psychosocial Outcomes from Baseline to Postintervention in the LIFTING Trial

Outcome	Baseline	Postintervention	Median Change (95% CI)	p value
	Median (IQR)	Median (IQR)		
Head and Neck Symptom Index	11.0 (9.4 to 13.8)	11.0 (9.0 to 12.8)	-0.29 (-3.0 to +1.8)	0.67
Neck Dissection Impairment	81.3 (75.2 to 94.4)	83.8 (76.3 to 94.4)	0 (-6.3 to +6.3)	0.83
Symptom Assessment	8.0 (5.0 to 9.0)	10.8 (2.3 to 18.0)	+3.1 (-1.0 to +6.7)	0.09
Post Traumatic Growth	66.0 (24.0 to 73.3)	67.2 (45.8 to 75.0)	+3.3 (-11.8 to +26.8)	0.57
Fear of Cancer Recurrence	12.0 (6.0 to 17.0)	14.0 (5.3 to 20.0)	+1.3 (-3.0 to +6.0)	0.29
Fatigue	3.0 (1.3 to 9.8)	2.0 (0.3 to 10.0)	-0.3 (-2.0 to +2.0)	0.58
Anxiety	14.0 (10.0 to 16.8)	11.0 (10.0 to 15.8)	-1.5 (-4.0 to +1.0)	0.34
Stress	11.0 (9.0 to 17.0)	11.0 (9.0 to 15.8)	+1.3 (-4.0 to +5.5)	0.83
Self-Esteem	40.0 (30.3 to 40.0)	39.0 (29.3 to 40.0)	-0.3 (-1.5 to +1.0)	0.49
Sleep Quality	5.0 (0.8 to 7.0)	4.0 (2.3 to 6.3)	0 (-2.5 to 2.0)	0.75

IQR=interquartile range, 25th and 75th percentiles

Table 12. Changes in Motivational and Behavioural Outcomes from Baseline to Postintervention in the LIFTING Trial

Variable (n=8)	Baseline	Postintervention	Median Change (95% CI)	p value
	Median (IQR)	Median (IQR)		
Beneficial	5.0 (4.3 to 5.0)	5.0 (5.0 to 5.0)	0 (-0.5 to +0.5)	0.56
Enjoyable	5.0 (4.0 to 5.0)	5.0 (5.0 to 5.0)	0 (0 to +1.0)	0.18
Supported	5.0 (5.0 to 5.0)	5.0 (5.0 to 5.0)	0 (0 to +0.5)	0.31
Motivated	5.0 (5.0 to 5.0)	5.0 (5.0 to 5.0)	0 (0)	1.00
Difficulty	3.0 (2.0 to 3.0)	2.0 (1.0 to 2.8)	-1 (-1.5 to 0)	0.84
Control	5.0 (4.0 to 5.0)	5.0 (3.3 to 5.0)	0 (-1.0 to +1.0)	1.00
Confidence	5.0 (4.3 to 5.0)	5.0 (5.0 to 5.0)	0 (-0.5 to +0.5)	0.56
Aerobic Exercise (minutes/week)	258 (79 to 594)	268 (214 to 608)	+150 (-128 to +527)	0.12
Non-Trial Weight Training (minutes/week)	0 (0 to 104)	140 (63 to 180)	+67 (-15 to +170)	0.12

Evaluations for all motivation questions were on a 5-point scale (1 = not at all, 2 = a little bit, 3 = somewhat, 4 = quite a bit, 5 = very much). IQR=interquartile range, 25th and 75th percentiles.

Table 13. Perceived Benefits of Heavy Lifting Strength Training in the LIFTING Trial

Benefits (n=8)	Mean (SD)	Worse: 1-3 n (%)	No Change: 4 n (%)	Better: 5-7 n (%)
Physical Fitness	6.9 (0.4)			8 (100%)
Ability to stop thinking about your cancer	5.6 (1.4)		3 (37.5%)	5 (62.5%)
Sense of control over your health	6.5 (1.1)		1 (12.5%)	7 (87.5%)
Muscular strength	7.0 (0)			8 (100%)
Shoulder/neck pain or injury	5.1 (1.5)	1 (12.5%)	2 (25%)	5 (62.5%)
Shoulder/neck motion	5.3 (1.5)	1 (12.5%)	2 (25%)	5 (62.5%)
Fatigue to carry out daily activities	5.8 (1.2)		1 (12.5%)	7 (87.5%)
Fear of cancer recurrence	4.9 (1.6)	1 (12.5%)	4 (50%)	3 (37.5%)
Overall quality of life	6.1 (1.1)		1 (12.5%)	7 (87.5%)

Evaluations for all questions were on 7-point scale (1 = very much worse, 2 = somewhat worse, 3 = slightly worse, 4 = no change, 5 = slightly better, 6 = somewhat better, 7 = very much better).

Table 14. Perceived Barriers to Heavy Lifting Strength Training in the LIFTING Trial

Barriers (n=8)	Mean (SD)	Not At All: 1-2 n (%)	Somewhat: 3-5 n (%)	Very Much: 6-7 n (%)
Having head and neck cancer	1.5 (1.4)	6 (75%)	2 (25%)	
Fear of cancer recurrence	0.3 (0.5)	8 (100%)		
Shoulder/neck pain	1.0 (1.1)	7 (87.5%)	1 (12.5%)	
Muscle/joint injury	1.1 (1.12)	7 (87.5%)	1 (12.5%)	
Bad weather	0.3 (0.5)	8 (100%)		
Medical appointments	0.3 (0.5)	8 (100%)		
Feeling tired/fatigued	0.3 (0.5)	8 (100%)		
Lack of motivation	0.1 (0.4)	8 (100%)		
Too busy/lack of time	0.1 (0.4)	8 (100%)		
Muscle/joint pain or soreness	0.6 (0.9)	8 (100%)		
Feeling sick/unwell	0.1 (0.4)	8 (100%)		
Travelling to facility	0.3 (0.5)	8 (100%)		
Exercise program was too hard	0.4 (0.5)	8 (100%)		

Evaluations for all questions were on a 7-point scale (1-2 = not at all, 3-5 = somewhat/a fair bit, 6-7 = very much).

Table 15. Motivation to Continue Heavy Lifting Strength Training After the LIFTING Trial

Variable	Mean (SD)	Not At All: 1 n (%)	A Little Bit: 2 n (%)	Somewhat: 3 n (%)	Quite A Bit: 4 n (%)	Very Much: 5 n (%)
Beneficial (n=7)	5.0 (0)					7 (100%)
Enjoyable (n=7)	3.9 (0.9)			3 (42.8%)	2 (28.5%)	2 (28.5%)
Supported (n=7)	4.1 (0.9)			2 (28.5%)	2 (28.5%)	3 (42.8%)
Motivated (n=7)	4.4 (1.0)			2 (28.5%)		5 (71.4%)
Difficulty (n=7)	2.6 (0.8)		4 (57.1%)	2 (28.5%)	1 (14.2%)	
Controllability (n=7)	4.1 (1.2)		1 (14.2%)	1 (14.2%)	1 (14.2%)	4 (57.1%)
Confidence (n=8)	3.4 (1.6)	2 (25%)		1 (12.5%)	3 (37.5%)	2 (25%)
Detailed Plan (n=8)	2.9 (1.7)	3 (37.5%)		2 (25%)	1 (12.5%)	2 (25%)

Evaluations for all motivation questions were on a 5-point scale (1 = not at all, 2 = a little bit, 3 = somewhat, 4 = quite a bit, 5 = very much).

FIGURES

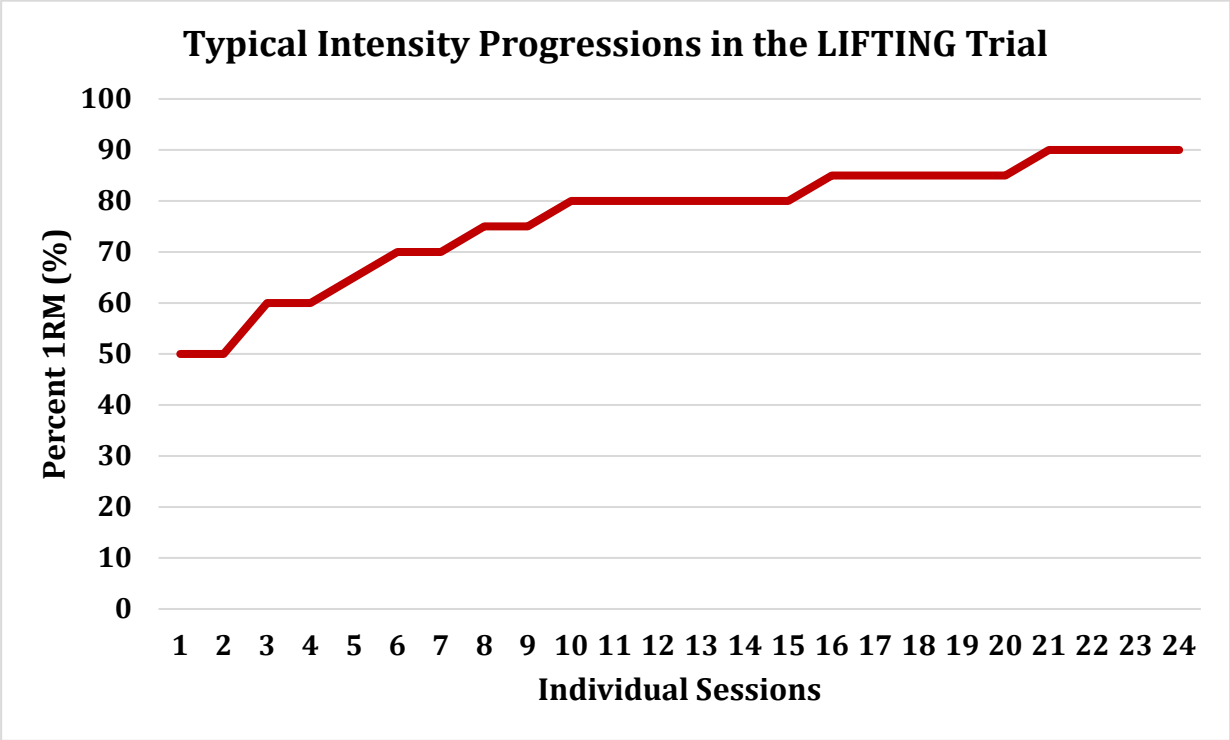
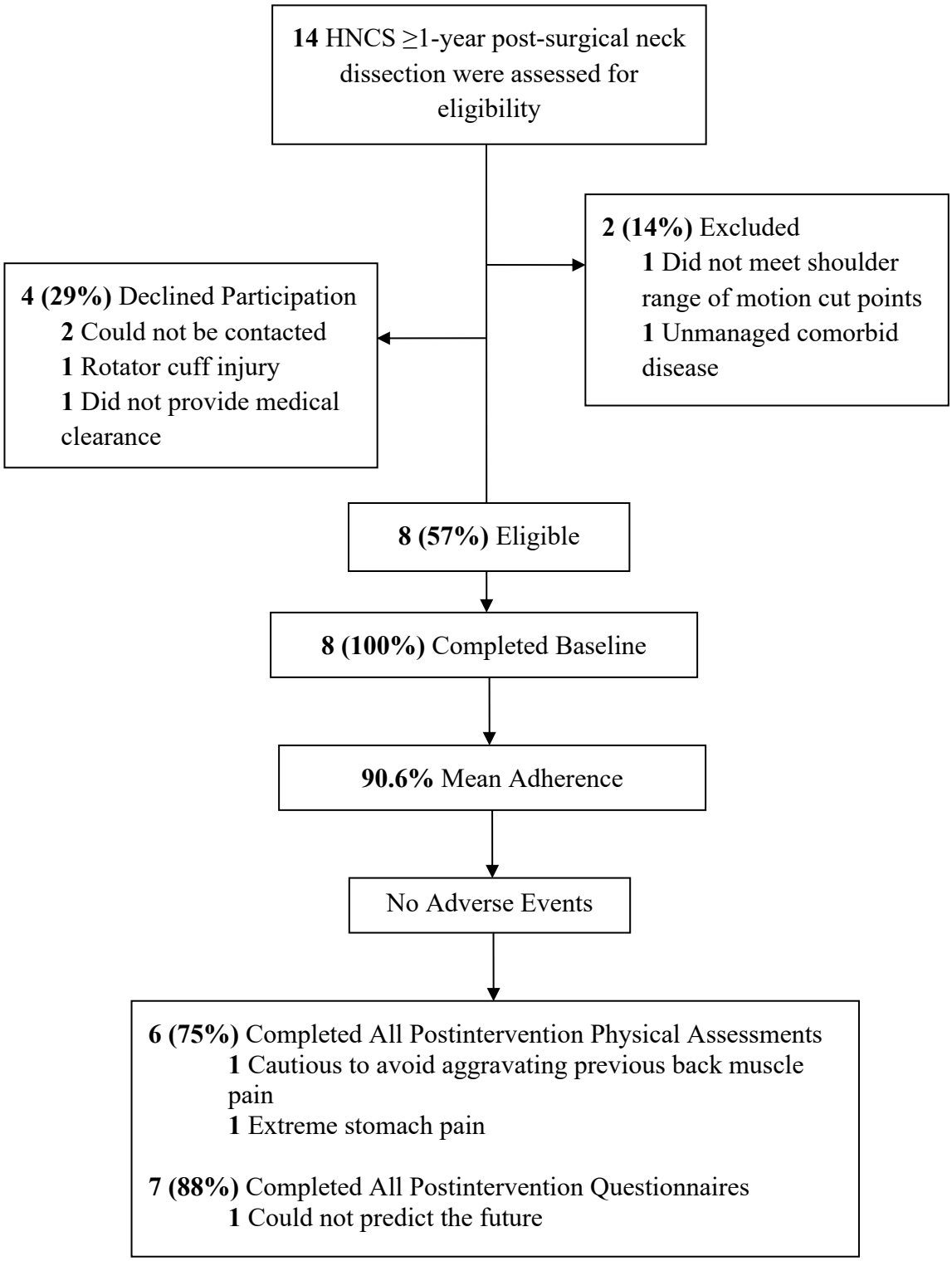


Figure 1. Typical Intensity Progressions in the LIFTING Trial

Figure 2. CONSORT Flow Diagram



CHAPTER FOUR

DISCUSSION

Overview

In this section, I expand on some of the key discussion points related to strength and limitations of the study, and future research directions.

Strengths and Limitations

The LIFTING trial has important strengths and limitations that will be elaborated on below. To the best of my knowledge, this was the first study to test the feasibility and safety of a HLST program in HNCS 1-year post-surgical ND. This is an important strength because the response to exercise may be different due to specific disease, treatment, and demographic variables. As such, we may not be able to generalize the benefits and harms of exercise from one patient population to another. This study may inform future research in this cancer group moving forward, and shed light on areas that have not been explored before.

The supervised component of the LIFTING trial was an important strength of the study for the safety of the participants and because HLST was new to all participants, and required proper coaching. All adverse events, modifications, and reasons for missed sessions were carefully tracked and reported. This is crucial to understand the benefits, harms, and barriers of any experimental exercise intervention in a particular patient group, and will help in the design of phase II trials in HNCS.

Each HLST program was individualized based on baseline test scores, previous exercise experience, restrictions, past/current injuries, form, and comfort with the exercises. Although a general exercise prescription was developed **(Tables 2 and 3),** adjustments were made regularly to best suit the abilities of each participant. Overhead pressing movements were completely avoided for all as they have been associated with higher levels of trapezius muscle

activity in patients with accessory nerve injury following ND surgery (41), and loaded overhead exercises might have caused pain or discomfort with a lack of trapezius activation in this cancer group.

Lastly, validated measures were used to assess health-related fitness and patient-reported outcomes as well as backup plans for maximal testing and exercise modifications in case these needed to be utilized. As a whole, 1RM testing was feasible in the LIFTING trial. However, future trials that plan to utilize the 1RM test should consider evidence-based motivational strategies to encourage study participants to continue to approach their true 1RM. In addition, familiarization sessions prior to 1RM testing may be unnecessary. A systematic review suggested that the 1RM has good to excellent test-retest reliability regardless of resistance training experience, number of familiarization sessions, exercise selection, upper versus lower body assessment, sex and age of participants (79). In addition, for older adults (mean: 70.7 years), 1RM prediction equations underestimate the actual 1RM (73).

One key limitation of this study is the small sample size. Consequently, the feasibility data reported from the LIFTING trial may not entirely reliable and should be interpreted with caution, as it may not be appropriate to generalize across all HNCS post-ND.

A second limitation is the lack of a comparison group such as moderate or light intensity resistance training. Without a comparison group, we were unable to comment on whether components of the HLST may have been the key factor that improved strength and global health status/quality of life. In addition, we were unable to conclude what exercise intensity may be optimal for HNCS.

Additionally, variations in age, HNC subtype, adjuvant treatment received, time since ND were present, making this patient group a heterogenous sample. The HNCS in the LIFTING trial were fairly high functioning at baseline and post HLST based on self-reported

functional and symptom scores, as well as motivational and behavioural outcomes. Therefore, recruitment bias of the LIFTING trial may have been more appealing to high functioning HNCS. It is not advised to generalize the results of the LIFTING trial to all HNCS.

Given that this study was part of a 2-year master's thesis, the recruitment period was limited to 8 months. Since convenience sampling was used to recruit participants, we were unable to track how many HNCS in the two clinics were screened, deemed ineligible, approached, or declined. Unfortunately, the LIFTING trial was conducted during the COVID-19 pandemic, which greatly impacted recruitment and data collection. This meant that the study coordinator could not recruit in-person in the clinic setting. This served as a limitation as some potential participants were hesitant to enroll in any in-person activities due to fear of contracting the virus. However, it is difficult to know exactly the degree of impact the pandemic had on the recruitment and data collection stages of the trial.

Another limitation of the study was the lack of postintervention follow-up to examine continuation of exercise, diminishing returns, or how long it takes for gains to begin reversing. However, given the timeframe of a master's program, this was not feasible. Another important limitation of the study was the estimation of 1RM for 2 participants from 3RM and 2RM; one estimation was made for the squat in one participant, and the other for the deadlift in another participant, respectively. This is an important limitation to the study because 1RM prediction equations are not entirely accurate, and tend to underestimate the actual 1RM in older adults (73). Another limitation of the LIFTING trial was the use of a self-reported measure to assess physical activity levels. Self-reported data is a limitation because it introduces the possibility of responses that are exaggerated or underestimated, and participants may misinterpret the questions. For all results from the LIFTING trial, it is important to note that these should not be

generalized to other patient populations as the response to exercise may differ based on disease and treatment variables (74).

Future Directions

Trials are needed that accurately track eligibility and recruitment rates. This is crucial to inform future studies about what is feasible in terms of monthly or yearly recruitment rates of HNCS into an exercise trial. In addition, difficulties with recruitment may have serious consequences for the rest of the trial such as a limited sample size, having to increase the duration of recruitment, or expanding the eligibility criteria mid-trial. A long-lasting trial may also delay many HNCS from having access to a promising exercise intervention.

Studies with larger sample sizes are necessary to increase the integrity and validity of the findings. If studies with small sample sizes continue to be published in HNCS, there may be a higher chance of finding no significant differences in various variables post HLST and other exercise interventions, when significant differences may actually exist but were not detected. In addition, results from larger studies are more appropriate to generalize to HNCS as a whole.

In addition, randomized controlled trials with comparison groups are warranted. Without a proper comparison group, it is unknown if changes in outcomes may have occurred just based on time, other life events, or learning. Moreover, it is unknown if the maintenance of an outcome (no change) in the intervention group may actually be a benefit because it is possible that the comparison group might have declined over time (gotten worse). These trials will aid in establishing the efficacy of HLST and its impact on health-related fitness and patient-reported outcomes such as muscular strength, physical functioning, quality of life, post traumatic growth, fear of cancer recurrence, pain, body composition, anxiety, fatigue, stress, shoulder mobility, self-esteem, and sleep quality. In addition, HLST can be compared to no

exercise, MLST, and/or an aerobic exercise group to assess for the changes in physical and psychosocial outcomes.

Future trials should also consider the addition of other outcomes such as cardiorespiratory function, dietary pattern and nutrient intake (ie. liquid or solid food diet, protein intake), duration required to return to work and normal daily activities, and post-surgical complications. Surgical site infections are associated with an increased risk of mortality, morbidity, and longer hospital stays post HNC surgery (8). Therefore, side effects may vary based on whether HNCS have experienced post-surgical complications and depending on which type of ND was received (radical, modified, or selective). This information may inform the development of individual exercise prescriptions and appropriate modifications.

In addition, future research should assess for changes in radiation-induced fibrosis via CT scan which will show abnormalities in soft tissue structures (74), and function of the SAN via electromyography before and after a HLST intervention to evaluate whether exercise may have an impact on fibrous tissues or SAN function. In addition, any type of ND leads to fibrosis, or a feeling of stiffness and constriction in the neck (35).

Furthermore, future trials may evaluate the manipulation of exercise prescription variables (frequency, intensity, time, type, volume, and progression) of the HLST to determine the optimal dose for improving health-related fitness and patient-reported outcomes. In addition, HLST can be compared to light-to-moderate resistance training to help determine the optimal exercise intensity and type for HNCS.

Ideally, future HLST intervention will be longer in duration with long-term follow-up, in order to assess if and when gains from the HLST program start to return to baseline levels. HLST interventions that are longer in duration should also consider a built-in ankle, hip, and

shoulder mobility program prior to using barbells to avoid limitations in movement due to mobility restrictions.

Lastly, keeping in mind the debilitating effects of HNC treatments, future research should consider HLST in the prehabilitation setting for HNC patients in hopes of minimizing and/or preventing various acute and chronic deficits. It is important to maximize muscle strength and function pre-ND because during an ND, the SCM and SAN may be removed. This leads to significant negative effects on daily activities, work, and leisure for HNCS of NDs (35). However, debilitating side effects are reported in all ND types. Substantially more research is needed before specific exercise recommendations for HNCS post-surgical ND can be made.

Conclusions

In conclusion, preliminary data from the LIFTING trial suggests that a supervised HLST exercise intervention in HNCS post-surgical ND is potentially safe, feasible, and well-received by participants. Although this phase I study experienced challenges with recruitment, it demonstrated excellent adherence, follow-up rates, strength gains, and improvements in global health status/quality of life ≥1-year post-ND in those who did participate. The LIFTING trial also provides important information to inform the development of future trials. Larger phase II trials in HNCS post-ND with a comparison group are necessary to examine the effects of HLST on health-related fitness and patient-reported outcomes. If HLST is shown to be beneficial, this method of training could be considered for HNCS to return to work, and manage and/or minimize various surgical-related side effects, and improve outcomes.

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Appendix A. Data Collection Sheet

Study ID (initials): Date:
Timepoint: (dd/mmm/yyyy)
Duration:

Physical Assessment Worksheet

Important Information

	Notes
Age	
Exercise Contraindications	
Medications	
Past/Current Injuries	
Additional Notes Prior to Testing	

Resting Measurements

1. **Blood Pressure:** _____mmHg
   Normal: resting blood pressure: <160/<90 mmHg

2. **Heart Rate:** _____bpm
   Normal resting heart rate: 60-100 bpm

3. **Waist to Hip Ratio**
   Hips (trial 1 cm): _____ Hips (trial 2 cm): _____ Average (cm): _____

   Waist (trial 1 cm): _____ Waist (trial 2 cm): _____ Average (cm): _____

   Ratio (waist/hip): _____

4. **Height:** _____inches _____cm **5. Weight:** _____kg _____lbs

Ranges of Motion

1. **Active Shoulder Flexion**

	Right (°)	Left (°)
Trial 1		
Trial 2		
Average (°)		

- *EXCLUDE if:*
    - *18-50 years: <150°*
    - *Over 50 years: <130°*

2. Active Shoulder ABduction

	Right (°)	**Left (°)**
Trial 1		
Trial 2		
Average (°)		

- *EXCLUDE if:*
    - *18-50 years: <150°*
    - *Over 50 years: <130°*

Physical Assessments

1. **Final Squat RPE:** _____ **1RM Weight:** _____lbs
    a. 1st Max Attempt at RPE 9-10 (lbs): _____
    b. 2nd Max Attempt at RPE 9-10 (lbs): _____
    c. 3rd Max Attempt at RPE 9-10 (lbs): _____

Testing Progressions

Target Intensity (% Body Weight)	**Target Repetitions**	**Actual Repetitions**	**Weight (lbs)**	**RPE**
Empty Barbell (or body weight)	8-10			
50%= lbs	5-6			
70%= lbs	2-3			
85%= lbs	1			
90%= lbs	1			
95%= lbs	1			
100%+ = lbs	1			

Notes:

_____
_____
_____
_____
_____

2. Final Bench Press 1 RM weight: _____lbs

a. 1st Max Attempt at RPE 9-10 (lbs): _____

b. 2nd Max Attempt at RPE 9-10 (lbs): _____

c. 3rd Max Attempt at RPE 9-10 (lbs): _____

Testing Progressions

Target Intensity (% Body Weight)	**Target Repetitions**	**Actual Repetitions**	**Weight (lbs)**	**RPE**
Empty barbell (or dumbbells less than 35% body weight)	8-10			
35%= lbs	5-6			
40%= lbs	2-3			
45%= lbs	1			
50%+ = lbs	1			

Notes:

_____
_____
_____
_____
_____

3. Final Conventional Deadlift RPE: _____ 1RM Weight: _____lbs

a. 1st Max Attempt at RPE 9-10 (lbs): _____

b. 2nd Max Attempt at RPE 9-10 (lbs): _____

c. 3rd Max Attempt at RPE 9-10 (lbs): _____

Testing Progressions

Target Intensity (% Body Weight)	**Target Repetitions**	**Actual Repetitions**	**Weight (lbs)**	**RPE**
Empty Barbell (or body weight)	8-10			
50%= lbs	5-6			
70%= lbs	2-3			
85%= lbs	1			
90%= lbs	1			
95%= lbs	1			
100%+ = lbs	1			

Notes:

_____
_____
_____
_____
_____

Post-Exercise Measurements (after stretching)

1. **Blood Pressure:** _____mmHg
2. **Heart Rate:** _____bpm

Additional Fitness Tests (for 50 years and older ONLY)

1. **Sit to Stand** repetitions in 30 seconds: _____
2. **6 minute walk test:**

a. # of laps completed _____ b. Partial distance completed _____m

c. Total Distance _____m

Distance (metres) = (# lengths completed x walkway distance) + partial distance on final length
1 lap=30 metres

Additional Notes

_____
_____
_____
_____
_____
_____
_____
_____
_____
_____

Appendix B. Exercise Log

INTERVENTION TRACKING SHEET

Study ID: [Subject] **Initials:** [Title]

Comorbidities/Medical Conditions	Status	Treatment/Medication Note

INTERVENTION TRACKING SHEET

Study ID: [Subject] **Initials:** [Title]

Week /Day #	Date / Day (MM-DD)		Pre-Exercise Screening					Post-Exercise Evaluation				
			Resting HR (bpm)	**Resting BP** (mmHg)	**Resting Fatigue** (1-10)	**Resting Pain** (1-10)	**Note**	**RPE Main Move-ments** (0-10)	**Fatigue** (1-10)	**Pain** (1-10)	**Program modification & reason?**	**Total Session Time** (mins)
5-1		M T W T F S S		/								
5-2		M T W T F S S		/								
6-1		M T W T F S S		/								
6-2		M T W T F S S		/								
7-1		M T W T F S S		/								
7-2		M T W T F S S		/								
8-1		M T W T F S S		/								
8-2		M T W T F S S		/								

Week /Day #	Date / Day (MM-DD)		Pre-Exercise Screening					Post-Exercise Evaluation				
			Resting HR (bpm)	**Resting BP** (mmHg)	**Resting Fatigue** (1-10)	**Resting Pain** (1-10)	**Note**	**RPE Main Move-ments** (0-10)	**Fatigue** (1-10)	**Pain** (1-10)	**Program modification & reason?**	**Total Session Time** (mins)
9-1		M T W T F S S		/								
9-2		M T W T F S S		/								
10-1		M T W T F S S		/								
10-2		M T W T F S S		/								
11-1		M T W T F S S		/								
11-2		M T W T F S S		/								
12-1		M T W T F S S		/								
12-2		M T W T F S S		/								

Appendix C. Baseline Questionnaire

Identification #: Date:

Feasibility and Safety of Heavy Lifting Strength Training in Head and Neck Cancer Survivors Post-Surgical Neck Dissection:
The LIFTING Trial

Stephanie Magdaline Ntoukas, BKin; Margaret L. McNeely, PhD; Hadi Seikaly, MD, FRCSC; Daniel A. O'Connell, MD, FRCSC; Kerry S. Courneya, PhD

BASELINE QUESTIONNAIRE

Instructions

Thank you for agreeing to participate in this study. In this questionnaire, we are going to ask you a series of questions about yourself. Many of the questions ask you about your physical and mental health, and some may be viewed as personal. It is important to answer as many of these questions as possible. However, if you feel uncomfortable answering certain questions please leave them blank. All responses are completely confidential and will never be used in any way that could link them to you. Many of the questions may seem similar but it is important to treat each question separately and provide an answer for each. There are no right or wrong answers and all we ask is that you provide responses that are as honest and accurate as possible. The questionnaire should take about 30-45 minutes of your time to complete.

If you have any questions, please do not hesitate to contact Stephanie Ntoukas (Study Coordinator) at: (780) 492-2829 or ntoukas@ualberta.ca.

The following questions pertain to you and your health and well-being. Please answer all questions yourself by circling the number that best applies to you. There are no 'right' or 'wrong' answers. Please circle one number between 0 and 3 that is most applicable to you. The information that you provide will remain strictly confidential.

	Not at all	A little	Quite a bit	Very much
1. Do you have trouble doing strenuous activities (example: carrying heavy shopping bags or a suitcase)?	0	1	2	3
2. Do you have any trouble taking a long walk?	0	1	2	3
3. Do you have any trouble taking a short walk outside of the house?	0	1	2	3
4. Do you need to stay in bed or in a chair during the day?	0	1	2	3
5. Do you need help with eating, getting dressed, washing yourself, or using the washroom?	0	1	2	3

During the <u>PAST WEEK:</u>	Not at all	A little	Quite a bit	Very much
6. Were you physically limited in doing your work or other daily activities?	0	1	2	3
7. Were you limited in pursuing your hobbies or other leisure activities?	0	1	2	3
8. Were you short of breath?	0	1	2	3
9. Have you had pain?	0	1	2	3
10. Did you need to rest?	0	1	2	3
11. Have you had trouble sleeping?	0	1	2	3
12. Have you felt weak?	0	1	2	3
13. Have you lacked an appetite?	0	1	2	3
14. Have you felt nauseous?	0	1	2	3

15. Have you vomited?	0	1	2	3
16. Have you been constipated?	0	1	2	3

During the <u>PAST WEEK:</u>	Not at all	A little	Quite a bit	Very much
17. Have you had diarrhea?	0	1	2	3
18. Were you tired?	0	1	2	3
19. Did pain interfere with your daily activities?	0	1	2	3
20. Have you experienced difficulties with concentration (examples: reading the newspaper or watching television)?	0	1	2	3
21. Did you feel tense?	0	1	2	3
22. Did you worry?	0	1	2	3
23. Did you feel irritable?	0	1	2	3
24. Did you feel depressed?	0	1	2	3
25. Have you had difficulty remembering things?	0	1	2	3
26. Has your physical condition interfered with your <u>family</u> life?	0	1	2	3
27. Has your physical condition interfered with your <u>social</u> activities?	0	1	2	3
28. Has your physical condition or cancer treatment caused you financial difficulties?	0	1	2	3

For the following questions, please circle one number between 1 and 7 that is most applicable to you.

29. How would you rate your overall <u>health</u> during the <u>past week?</u>

1	2	3	4	5	6	7
Very poor						Excellent

30. How would you rate your overall <u>quality of life</u> during the <u>past week?</u>

1	2	3	4	5	6	7

Very poor Excellent

This first set of questions asks about how your diagnosis and treatment for head and neck cancer may have changed your life. Please circle the number that best represents the **degree to which your life** has changed **as a result of being diagnosed and treated for head and neck cancer. Please use the following scale to guide your responses.**

0	**1**	**2**	**3**	**4**	**5**
Did not experience a change	**Changed to a very small degree**	**Changed to a small degree**	**Changed to a moderate degree**	**Changed to a great degree**	**Changed to a very great degree**

After being diagnosed and treated for head and neck cancer…

1. I changed my priorities about what is important in life.

0 1 2 3 4 5

2. I have a greater appreciation for the value of my own life.

0 1 2 3 4 5

3. I developed new interests.

0 1 2 3 4 5

4. I have a greater feeling of self-reliance.

0 1 2 3 4 5

5. I have a better understanding of spiritual matters.

0 1 2 3 4 5

6. I more clearly see that I can count on people in times of trouble.

0 1 2 3 4 5

7. I established a new path for my life.

0 1 2 3 4 5

8. I have a greater sense of closeness with others.

0 1 2 3 4 5

9. I am more willing to express my emotions.

0 1 2 3 4 5

10. I know better that I can handle difficulties.

0 1 2 3 4 5

11. I am able to do better things with my life.

0 1 2 3 4 5

After being diagnosed and treated for head and neck cancer…

12. I am better able to accept the way things work out.

0 1 2 3 4 5

13. I can better appreciate each day.

0 1 2 3 4 5

14. New opportunities are available which wouldn't have been otherwise.

0 1 2 3 4 5

15. I have more compassion for others.

0 1 2 3 4 5

16. I put more effort into my relationships.

0 1 2 3 4 5

17. I am more likely to try to change things that need changing.

0 1 2 3 4 5

18. I have a stronger religious faith.

0 1 2 3 4 5

19. I discovered that I'm stronger than I thought I was.

0 1 2 3 4 5

20. I learned a great deal about how wonderful people are.

0 1 2 3 4 5

21. I better accept needing others.

0 1 2 3 4 5

A large number of people who have received a head and neck cancer diagnosis are concerned to varying degrees, that their cancer may recur. A **cancer recurrence involves the presence**

of cancer in the same region or a different region of the body. The following questions will be useful in understanding the experience of concerns regarding a cancer recurrence. Please read each statement and circle the appropriate number to indicate to what degree it has applied to you **during the past month.**

0 Not at all	**1** A little	**2** Somewhat	**3** A lot	**4** A great deal

1.	I am worried or anxious about the possibility of cancer recurrence	0	1	2	3	4
2.	I am afraid of cancer recurrence	0	1	2	3	4
3.	I believe it is normal to be worried or anxious about the possibility of cancer recurrence	0	1	2	3	4
4.	When I think about the possibility of cancer recurrence, this triggers other unpleasant thoughts or images (ie. death, suffering, the consequences for my family)	0	1	2	3	4
5.	I believe that I am fine and that the cancer will not recur	0	1	2	3	4

6. In your opinion, are you at risk of having a cancer recurrence?

0	1	2	3	4
Not at all at risk	A little risk	Somewhat at risk	A lot at risk	A great deal at risk

7. How often do you think about the possibility of cancer recurrence?

0	1	2	3	4
Never	A few times a month	A few times a week	A few times a day	Several times a day

8. How much time **per day** do you spend thinking about the possibility of cancer recurrence?

0	1	2	3	4
I don't think about it	A few seconds	A few minutes	A few hours	Several hours

9. How long have you been thinking about the possibility of cancer recurrence?

0	1	2	3	4
I don't think about it	A few weeks	A few months	A few years	Several years

Below is a list of statements that other people with your illness have said are important. Please circle or mark one number per line to indicate your response as it applies to the **past 7 days.**

	Not at all	A little	Quite a bit	Very much
1. I have pain	0	1	2	3
2. I have a lack of energy	0	1	2	3
3. I can swallow naturally and easily	0	1	2	3
4. I have pain in my mouth, throat, or neck	0	1	2	3
5. I have trouble breathing	0	1	2	3
6. I am able to communicate with others	0	1	2	3
7. I have nausea	0	1	2	3
8. I can eat solid foods	0	1	2	3
9. I worry that my condition will get worse	0	1	2	3
10. I am content with the quality of my life right now	0	1	2	3

A number of statements which people have used to describe themselves are given below. Read each statement and circle the appropriate number that best indicates how you have felt **during the past week.**

During the PAST WEEK	Not at all	Somewhat	Moderately so	Very much so
I feel calm	1	2	3	4
I am tense	1	2	3	4
I feel at ease	1	2	3	4
I am presently worrying over possible misfortunes	1	2	3	4
I feel frightened	1	2	3	4
I feel self-confident	1	2	3	4
I am jittery	1	2	3	4
I feel indecisive	1	2	3	4
I am relaxed	1	2	3	4
I am worried	1	2	3	4
I feel steady	1	2	3	4

Below is a list of statements that other people with your illness have said are important. Please circle or mark one number per line to indicate your response as it applies to the **past 7 days.**

	Not at all	A little bit	Somewhat	Quite a bit	Very much
1. I feel fatigued	0	1	2	3	4
2. I feel weak all over	0	1	2	3	4
3. I feel listless ('washed out')	0	1	2	3	4
4. I feel tired	0	1	2	3	4
5. I have trouble starting things because I am tired	0	1	2	3	4
6. I have trouble finishing things because I am tired	0	1	2	3	4
7. I have energy	0	1	2	3	4
8. I am able to do my usual activities	0	1	2	3	4
9. I need to sleep during the day	0	1	2	3	4
10. Am too tired to eat	0	1	2	3	4
11. I need help doing my usual activities.	0	1	2	3	4
12. I am frustrated by being too tired to do the things I want to do	0	1	2	3	4
13. I have to limit my social activity because I am tired	0	1	2	3	4

The next questions ask you about your feelings and thoughts **during the last month.** Although some of the questions are similar, there are differences between them and you should treat each one as a separate question. The best approach is to answer each one fairly quickly. For each question, please choose from the following alternatives:

In the LAST MONTH, how often have you…	Never	Almost never	Some-times	Fairly often	Very often
1. Been upset because of something that happened unexpectedly	0	1	2	3	4
2. Felt that you were unable to control the important things in your life	0	1	2	3	4
3. Felt nervous and stressed	0	1	2	3	4
4. Dealt successfully with irritating life hassles	0	1	2	3	4
5. Felt that you were effectively coping with important changes that were occurring in your life	0	1	2	3	4
6. Felt confident about your ability to handle your personal problems	0	1	2	3	4
7. Felt that things were going your way	0	1	2	3	4
8. Found that you could not cope with all the things that you had to do	0	1	2	3	4
9. Been able to control irritations in your life	0	1	2	3	4
10. Felt that you were on top of things	0	1	2	3	4
11. Been angered because of things that happened that were outside of your control	0	1	2	3	4
12. Found yourself thinking about things that you have to accomplish	0	1	2	3	4
13. Been able to control the way you spend your time	0	1	2	3	4
14. Felt difficulties were piling up so high that you could not overcome them	0	1	2	3	4

As a result of the cancer <u>treatment of your neck,</u> how much have you been bothered by the following over the **<u>past 4 weeks?</u>**

	Not at all	A little bit	A moderate amount	Quite a bit	A lot
1. Are you bothered by neck or shoulder **pain or discomfort?**	1	2	3	4	5
2. Are you bothered by neck or shoulder **stiffness?**	1	2	3	4	5
3. Are you bothered by difficulty with **self-care** activities because of your neck or shoulder (e.g., combing hair, dressing, bathing, etc)	1	2	3	4	5
4. Have you been limited in your ability to lift **light objects** because of your shoulder or neck?	1	2	3	4	5
5. Have you been limited in your ability to lift **heavy objects** because of your shoulder or neck?	1	2	3	4	5
6. Have you been limited in your ability to **reach above** for objects because of your shoulder or neck (e.g., from shelves, tables, or counters)?	1	2	3	4	5
7. Are you bothered by your **overall activity level** because of your shoulder or neck?	1	2	3	4	5
8. Has the treatment of your neck affected your participation in **social activities?**	1	2	3	4	5
9. Have you been limited in your ability to do **leisure or recreational** activities because of your neck or shoulder?	1	2	3	4	5
10. Have you been limited in your ability to do **work** (including **work at home**) because of your neck or shoulder?	1	2	3	4	5

The following questions will be used to assess the symptom burden that you experience. Please circle the number that best describes **how you feel NOW.**

No Pain	0	1	2	3	4	5	6	7	8	9	10	Worst Possible Pain
No Tiredness *(Tiredness = lack of energy)*	0	1	2	3	4	5	6	7	8	9	10	Worst Possible Tiredness
No Drowsiness *(Drowsiness = feeling sleepy)*	0	1	2	3	4	5	6	7	8	9	10	Worst Possible Drowsiness
No Nausea	0	1	2	3	4	5	6	7	8	9	10	Worst Possible Nausea
No Lack of Appetite	0	1	2	3	4	5	6	7	8	9	10	Worst Possible Lack of Appetitie
No Shortness of Breath	0	1	2	3	4	5	6	7	8	9	10	Worst Possible Shortness of Breath
No Depression *(Depression = feeling sad)*	0	1	2	3	4	5	6	7	8	9	10	Worst Possible Depression
No Anxiety *(Anxiety = feeling nervous)*	0	1	2	3	4	5	6	7	8	9	10	Worst Possible Anxiety
Best Wellbeing *(Wellbeing = how you feel overall)*	0	1	2	3	4	5	6	7	8	9	10	Worst Possible Wellbeing
No _____ Other Problem *(For example constipation)*	0	1	2	3	4	5	6	7	8	9	10	Worst Possible _____

The next questions concern the general perceptions that you currently have about yourself. Please circle the number that best reflects your current view of yourself using the following scale as a guide for your responses.

		Strongly Disagree	Disagree	Agree	Strongly Agree
1.	On the whole I am satisfied with myself	1	2	3	4
2.	At times I think that I am no good at all	1	2	3	4
3.	I feel that I have a number of good qualities	1	2	3	4
4.	I am able to do things as well as most other people	1	2	3	4
5.	I feel I do not have much to be proud of	1	2	3	4
6.	I certainly feel useless at times	1	2	3	4
7.	I feel that I am a person of worth, at least on an equal plane with others	1	2	3	4
8.	I wish I could have more respect for myself	1	2	3	4
9.	All in all, I am inclined to feel that I am a failure	1	2	3	4
10.	I take a positive attitude toward myself	1	2	3	4

For each question, please **CIRCLE** the number that best describes your sleep habits. Please rate the **CURRENT (i.e. LAST 2 WEEKS) SEVERITY** of your insomnia problem(s).

Insomnia Problem	None	Mild	Moderate	Severe	Very Severe
1. Difficulty falling asleep	0	1	2	3	4
2. Difficulty staying asleep	0	1	2	3	4
3. Problems waking up too early	0	1	2	3	4

4. How **SATISFIED/DISSATISFIED** are you with your **CURRENT** sleep pattern?

Very Satisfied	Satisfied	Moderately Satisfied	Dissatisfied	Very Dissatisfied
0	1	2	3	4

5. How **NOTICEABLE** to others do you think your sleep problem is in terms of impairing the quality of your life?

Not at all Noticeable	A Little	Somewhat	Much	Very Much Noticeable
0	1	2	3	4

6. How **WORRIED/DISTRESSED** are you about your current sleep problem?

Not at all Worried	A Little	Somewhat	Much	Very Much Worried
0	1	2	3	4

7. To what extent do you consider your sleep problem to **INTERFERE** with your daily functioning (e.g. daytime fatigue, mood, ability to function at work/daily chores, concentration, memory, mood, etc.) **CURRENTLY**?

Not at all Interfering	A Little	Somewhat	Much	Very Much Interfering
0	1	2	3	4

For this next question, we would like you to recall the amount of exercise you have done **during the past month.**

When answering these questions please:

- Only count exercise sessions that lasted 10 minutes or longer in duration.
- Only count exercise that was done during free time (i.e., not occupation or housework).
- Note that the main difference between the first three categories is the intensity of the endurance (aerobic) exercise and the fourth category is for strength (resistance) exercise.
- Write the average frequency on the first line and the average duration on the second.
- Write in "0" if you did not do any exercise in one of the categories.

Considering a **typical week (7-day period) over the past month,** how many times on average do you do the following kinds of exercise during your free time. Please write the appropriate number on each line.

AEROBIC EXERCISE	Times Per Week	Average Duration Per Session
a. VIGOROUS EXERCISE = *HEART BEATS RAPIDLY, SWEATING* (e.g., running, aerobics classes, cross country skiing, vigorous swimming, vigorous bicycling)	_____ times/week	_____ minutes/time
b. MODERATE EXERCISE = *NOT EXHAUSTING, LIGHT PERSPIRATION* (e.g., fast walking, tennis, easy bicycling, easy swimming, popular or folk dancing)	_____ times/week	_____ minutes/time
c. LIGHT EXERCISE = *MINIMAL EFFORT, NO PERSPIRATION* (e.g., easy walking, yoga, bowling, shuffleboard)	_____ times/week	_____ minutes/time
RESISTANCE/STRENGTH EXERCISE (e.g., weight lifting, push-ups, sit-ups, resistance band)	_____ times/week	_____ minutes/time

1. If you reported any resistance/strength exercise in the past month, how long have you been doing it? _____ months and _____ years

2. What type of resistance training exercises are you doing? Check all that apply.

Free Weights (ie. dumbbells, barbells)	☐	Machines	☐
Resistance Bands	☐	Body Weight Exercises	☐

The following questions ask you to rate how you feel about doing a **heavy lifting strength training (HLST) program.** Please pay careful attention to the words and descriptions for each scale and circle the number that best represents how you feel.

The HLST exercise program will begin with lighter weights that you can lift between 12 and 15 times before you are too tired. After you get used to the lighter weights, we will then ask you to try and lift very heavy weights that you can only lift 1 to 6 times before being too tired. The exercises we will ask you to do include: squat, bench press, deadlift, and accessory movements (e.g., lunges, face pulls, push-ups, planks, farmers carry). We will ask you to do this program 2 days per week for a total of 12 weeks at our fitness centre at the University of Alberta.

1. How beneficial do you think it will be for you to do this HLST program?

1	2	3	4	5
Not at all	A little bit	Somewhat	Quite a bit	Very much

2. How enjoyable do you think it will be for you to do this HLST program?

1	2	3	4	5
Not at all	A little bit	Somewhat	Quite a bit	Very much

3. How supportive do you think family/friends will be of you doing this HLST program?

1	2	3	4	5
Not at all	A little bit	Somewhat	Quite a bit	Very much

4. How motivated are you to do this HLST program?

1	2	3	4	5
Not at all	A little bit	Somewhat	Quite a bit	Very much

5. How difficult do you think it will be for you to do this HLST program?

1	2	3	4	5
Not at all	A little bit	Somewhat	Quite a bit	Very much

6. How much control do you think you will have over doing this HLST program?

1	2	3	4	5
Not at all	A little bit	Somewhat	Quite a bit	Very much

7. How confident are you that you will be able to do this HLST program?

1	2	3	4	5
Not at all	A little bit	Somewhat	Quite a bit	Very much

This important part of the questionnaire is needed to help understand the characteristics of the people participating in the study. All information is held in strict confidence and its presentation to the public will be group data only. It is important to answer as many of these questions as possible. However, if you feel uncomfortable answering certain questions, please leave them blank.

DEMOGRAPHIC

1. Age: _____

2. Sex: Female ☐ Male ☐

3. Current Marital Status:

Never Married	☐	Married	☐	Common Law	☐
Separated	☐	Widowed	☐	Divorced	☐

4. Education (Please check highest level attained):

Some High School	☐	Completed High School	☐
Some University/College	☐	Completed University/College	☐
Some Graduate School	☐	Completed Graduate School	☐

5. Annual Family Income:

< $20,000	☐	$20,000 – 39,999	☐
$40,000 – 59,999	☐	$60,000 – 79,999	☐
$80,000 – 99,999	☐	> $100,000	☐
		Prefer not to answer	☐

6. Current Employment Status: Full Time ☐ Part Time ☐ Sick Leave ☐ Retired ☐

   Temporarily off work ☐ Homemaker ☐ Disability ☐ Prefer not to answer ☐

7. What is your primary ethnic origin or race?

   White ☐ Black ☐ Hispanic ☐ Asian ☐ Aboriginal ☐
   Other_____

8. Which of the following best describes your current cigarette smoking status?

   Never Smoked Cigarettes ☐ Ex-Smoker ☐ Current Smoker ☐

9. Which of the following best describes your current alcohol consumption?

   Never Drink ☐ Social Drinker ☐ Regular Drinker (drink every day) ☐

MEDICAL

10. Has a doctor or nurse ever told you that you had any of the following conditions? (check all that apply):

Medical Conditions	Check if applicable, or leave blank if not applicable
Heart Disease or CVD	☐
Angina (chest pains)	☐
High Blood Pressure	☐
Stroke	☐
High Cholesterol	☐
Diabetes	☐
Arthritis, Osteoporosis, or Back Problems	☐
Asthma or COPD	☐
Spinal Cord Injury	☐
Other Cancer	☐
Any other long term health conditions: _____ _____ _____ _____	☐

11. In the past month, was your ability to exercise limited by a health condition, injury, or disability?

1	2	3	4	5
No, Not at All	A Little	Somewhat	Quite a lot	Completely

12. Are you currently taking any medications of health supplements for health problems? (e.g., blood pressure, anxiety, depression, pain, insomnia, etc).

What is the medication? (e.g., beta-blocker, Synthroid)	What is it for? (e.g., high blood pressure, hypothyroidism)	Dose (if known) (e.g., 50mg twice per day; 1 tablet per day)
1.		
2.		
3.		
4.		
5.		

Participant initials: _____

Questionnaire completion date: __ __ __ __ - __ __ - __ __
y y y y - m m - d d

Please feel free to make any additional comments concerning your head and neck cancer experience, the questionnaire, the exercise intervention, or anything else you think may be helpful to us or think we may have missed.

Appendix D. Postintervention Questionnaire

Identification #: Date:

Feasibility and Safety of Heavy Lifting Strength Training in Head and Neck Cancer Survivors Post-Surgical Neck Dissection:
The LIFTING Trial

Stephanie Magdaline Ntoukas, BKin; Margaret L. McNeely, PhD; Hadi Seikaly, MD, FRCSC; Daniel A. O'Connell, MD, FRCSC; Kerry S. Courneya, PhD

POST-INTERVENTION QUESTIONNAIRE

Instructions

Thank you for your continued participation in this study. At this post-intervention assessment, we are going to ask you many of the same questions as in the previous questionnaires. However, it is important to answer these questions based on what you are thinking and feeling right now and not on how you answered the questions last time. This will give us important information about how your thoughts and feelings have changed. Many of the questions may seem similar but it is important to treat each question separately and provide an answer for each. Also, if at all possible, it is important to answer all questions. However, if you feel uncomfortable answering certain questions please leave them blank. All responses are completely confidential and will never be used in any way that could link them to you. There are no right or wrong answers and all we ask is that you provide responses that are as honest and accurate as possible. The questionnaire should take about 30-45 minutes of your time to complete. If you have any questions about completing the questionnaire, please contact Stephanie Ntoukas (Study Coordinator) at (780) 492-2829 (call collect from out of town) or ntoukas@ualberta.ca.

The following questions pertain to you and your health and well-being. Please answer all questions yourself by circling one number between 0 and 3 that best applies to you. There are no 'right' or 'wrong' answers. The information that you provide will remain strictly confidential.

	Not at all	A little	Quite a bit	Very much
1. Do you have trouble doing strenuous activities (example: carrying heavy shopping bags or a suitcase)?	1	2	3	4
2. Do you have any trouble taking a long walk?	1	2	3	4
3. Do you have any trouble taking a short walk outside of the house?	1	2	3	4
4. Do you need to stay in bed or in a chair during the day?	1	2	3	4
5. Do you need help with eating, getting dressed, washing yourself, or using the washroom?	1	2	3	4

During the PAST WEEK:	Not at all	A little	Quite a bit	Very much
6. Were you physically limited in doing your work or other daily activities?	1	2	3	4
7. Were you limited in pursuing your hobbies or other leisure activities?	1	2	3	4
8. Were you short of breath?	1	2	3	4
9. Have you had pain?	1	2	3	4
10. Did you need to rest?	1	2	3	4
11. Have you had trouble sleeping?	1	2	3	4
12. Have you felt weak?	1	2	3	4
13. Have you lacked appetite?	1	2	3	4
14. Have you felt nauseous?	1	2	3	4
15. Have you vomited?	1	2	3	4

16. Have you been constipated?	1	2	3	4

During the PAST WEEK:	Not at all	A little	Quite a bit	Very much
17. Have you had diarrhea?	1	2	3	4
18. Were you tired?	1	2	3	4
19. Did pain interfere with your daily activities?	1	2	3	4
20. Have you experienced difficulties with concentration (examples: reading the newspaper or watching television)?	1	2	3	4
21. Did you feel tense?	1	2	3	4
22. Did you worry?	1	2	3	4
23. Did you feel irritable?	1	2	3	4
24. Did you feel depressed?	1	2	3	4
25. Have you had difficulty remembering things?	1	2	3	4
26. Has your physical condition or medical treatment interfered with your family life?	1	2	3	4
27. Has your physical condition interfered with your social activities?	1	2	3	4
28. Has your physical condition or medical treatment caused you financial difficulties?	1	2	3	4

For the following questions, please circle one number between 1 and 7 that is most applicable to you.

29. How would you rate your overall health during the past week?

1	2	3	4	5	6	7
Very poor						Excellent

30. How would you rate your overall quality of life during the past week?

1	2	3	4	5	6	7
Very poor						Excellent

This first set of questions asks about how your life has changed over the past three months. Please circle the number that best represents the **degree to which your life** has changed **over the past three months. Please use the following scale to guide your responses.**

0	1	2	3	4	5
Did not experience a change	**Changed to a very small degree**	**Changed to a small degree**	**Changed to a moderate degree**	**Changed to a great degree**	**Changed to a very great degree**

Over the past three months…

1. I changed my priorities about what is important in life.

0 1 2 3 4 5

2. I have a greater appreciation for the value of my own life.

0 1 2 3 4 5

3. I developed new interests.

0 1 2 3 4 5

4. I have a greater feeling of self-reliance.

0 1 2 3 4 5

5. I have a better understanding of spiritual matters.

0 1 2 3 4 5

6. I more clearly see that I can count on people in times of trouble.

0 1 2 3 4 5

7. I established a new path for my life.

0 1 2 3 4 5

8. I have a greater sense of closeness with others.

0 1 2 3 4 5

9. I am more willing to express my emotions.

0 1 2 3 4 5

10. I know better that I can handle difficulties.

0 1 2 3 4 5

11. I am able to do better things with my life.

0 1 2 3 4 5

Over the past three months…

12. I am better able to accept the way things work out

0 1 2 3 4 5

13. I can better appreciate each day.

0 1 2 3 4 5

14. New opportunities are available which wouldn't have been otherwise.

0 1 2 3 4 5

15. I have more compassion for others.

0 1 2 3 4 5

16. I put more effort into my relationships.

0 1 2 3 4 5

17. I am more likely to try and change things that need changing.

0 1 2 3 4 5

18. I have a stronger religious faith.

0 1 2 3 4 5

19. I discovered that I'm stronger than I thought I was.

0 1 2 3 4 5

20. I learned a great deal about how wonderful people are.

0 1 2 3 4 5

21. I better accept needing others

0 1 2 3 4 5

People who have had head and neck cancer diagnosis are concerned to varying degrees that their cancer may recur. A **cancer recurrence involves the presence of cancer in the same region or a different region of the body.** The following questions will be useful in understanding your concerns regarding a cancer recurrence. Please read each statement and circle the appropriate number to indicate to what degree it has applied to you **during the past month.**

0 Not at all	**1** A little	**2** Somewhat	**3** A lot	**4** A great deal

1.	I am worried or anxious about the possibility of cancer recurrence	0	1	2	3	4
2.	I am afraid of cancer recurrence	0	1	2	3	4
3.	I believe it is normal to be worried or anxious about the possibility of cancer recurrence	0	1	2	3	4
4.	When I think about the possibility of cancer recurrence, this triggers other unpleasant thoughts or images (ie. death, suffering, the consequences for my family)	0	1	2	3	4
5.	I believe that I am fine and that the cancer will not come back	0	1	2	3	4

6. In your opinion, are you at risk of having a cancer recurrence?

0	1	2	3	4
Not at all at risk	A little risk	Somewhat at risk	A lot at risk	A great deal at risk

7. How often do you think about the possibility of cancer recurrence?

0	1	2	3	4
Never	A few times a month	A few times a week	A few times a day	Several times a day

8. How much time **per day** do you spend thinking about the possibility of cancer recurrence?

0	1	2	3	4
I don't think about it	A few seconds	A few minutes	A few hours	Several hours

9. How long have you been thinking about the possibility of cancer recurrence?

0	1	2	3	4
I don't think about it	A few weeks	A few months	A few years	Several years

Below is a list of statements that other people with your illness have said are important. Please circle or mark one number per line to indicate your response as it applies to the **past 7 days.**

	Not at all	A little	Some-what	Quite a bit	Very much
1. I have pain	0	1	2	3	4
2. I have a lack of energy	0	1	2	3	4
3. I can swallow naturally and easily	0	1	2	3	4
4. I have pain in my mouth, throat, or neck	0	1	2	3	4
5. I have trouble breathing	0	1	2	3	4
6. I am able to communicate with others	0	1	2	3	4
7. I have nausea	0	1	2	3	4
8. I can eat solid foods	0	1	2	3	4
9. I worry that my condition will get worse	0	1	2	3	4
10. I am content with the quality of my life right now	0	1	2	3	4

A number of statements which people have used to describe themselves are given below. Read each statement and circle the appropriate number that best indicates how you have felt **during the past week.**

During the PAST WEEK	Not at all	Somewhat	Moderately so	Very much so
I feel calm	1	2	3	4
I am tense	1	2	3	4
I feel at ease	1	2	3	4
I am presently worrying over possible misfortunes	1	2	3	4
I feel frightened	1	2	3	4
I feel self-confident	1	2	3	4
I am jittery	1	2	3	4
I feel indecisive	1	2	3	4
I am relaxed	1	2	3	4
I am worried	1	2	3	4
I feel steady	1	2	3	4

Below is a list of statements that other people with your illness have said are important. Please circle or mark one number per line to indicate your response as it applies to the **past 7 days.**

	Not at all	A little bit	Somewhat	Quite a bit	Very much
1. I feel fatigued	0	1	2	3	4
2. I feel weak all over	0	1	2	3	4
3. I feel listless ('washed out')	0	1	2	3	4
4. I feel tired	0	1	2	3	4
5. I have trouble starting things because I am tired	0	1	2	3	4
6. I have trouble finishing things because I am tired	0	1	2	3	4
7. I have energy	0	1	2	3	4
8. I am able to do my usual activities	0	1	2	3	4
9. I need to sleep during the day	0	1	2	3	4
10. I am too tired to eat	0	1	2	3	4
11. I need help doing my usual activities.	0	1	2	3	4
12. I am frustrated by being too tired to do the things I want to do	0	1	2	3	4
13. I have to limit my social activity because I am tired	0	1	2	3	4

The next questions ask you about your feelings and thoughts **during the last month.** Although some of the questions are similar, there are differences between them and you should treat each one as a separate question. The best approach is to answer each one fairly quickly. For each question, please choose from the following alternatives:

In the LAST MONTH, how often have you…	Never	Almost never	Some-times	Fairly often	Very often
1. Been upset because of something that happened unexpectedly	0	1	2	3	4
2. Felt that you were unable to control the important things in your life	0	1	2	3	4
3. Felt nervous and stressed	0	1	2	3	4
4. Dealt successfully with irritating life hassles	0	1	2	3	4
5. Felt that you were effectively coping with important changes that were occurring in your life	0	1	2	3	4
6. Felt confident about your ability to handle your personal problems	0	1	2	3	4
7. Felt that things were going your way	0	1	2	3	4
8. Found that you could not cope with all the things that you had to do	0	1	2	3	4
9. Been able to control irritations in your life	0	1	2	3	4
10. Felt that you were on top of things	0	1	2	3	4
11. Been angered because of things that happened that were outside of your control	0	1	2	3	4
12. Found yourself thinking about things that you have to accomplish	0	1	2	3	4
13. Been able to control the way you spend your time	0	1	2	3	4
14. Felt difficulties were piling up so high that you could not overcome them	0	1	2	3	4

As a result of the cancer treatment of your neck, how much have you been bothered by the following over the **past 4 weeks?**

	Not at all	A little bit	A moderate amount	Quite a bit	A lot
1. Are you bothered by neck or shoulder **pain or discomfort?**	1	2	3	4	5
2. Are you bothered by neck or shoulder **stiffness?**	1	2	3	4	5
3. Are you bothered by difficulty with **self-care** activities because of your neck or shoulder (e.g., combing hair, dressing, bathing, etc)	1	2	3	4	5
4. Have you been limited in your ability to lift **light objects** because of your shoulder or neck?	1	2	3	4	5
5. Have you been limited in your ability to lift **heavy objects** because of your shoulder or neck?	1	2	3	4	5
6. Have you been limited in your ability to **reach above** for objects because of your shoulder or neck (e.g., from shelves, tables, or counters)?	1	2	3	4	5
7. Are you bothered by your **overall activity level** because of your shoulder or neck?	1	2	3	4	5
8. Has the treatment of your neck affected your participation in **social activities?**	1	2	3	4	5
9. Have you been limited in your ability to do **leisure or recreational** activities because of your neck or shoulder?	1	2	3	4	5
10. Have you been limited in your ability to do **work** (including **work at home**) because of your neck or shoulder?	1	2	3	4	5

The following questions will be used to assess the symptom burden that you experience. Please circle the number that best describes **how you feel NOW.**

No Pain	0	1	2	3	4	5	6	7	8	9	10	Worst Possible Pain
No Tiredness *(Tiredness = lack of energy)*	0	1	2	3	4	5	6	7	8	9	10	Worst Possible Tiredness
No Drowsiness *(Drowsiness = feeling sleepy)*	0	1	2	3	4	5	6	7	8	9	10	Worst Possible Drowsiness
No Nausea	0	1	2	3	4	5	6	7	8	9	10	Worst Possible Nausea
No Lack of Appetite	0	1	2	3	4	5	6	7	8	9	10	Worst Possible Lack of Appetitie
No Shortness of Breath	0	1	2	3	4	5	6	7	8	9	10	Worst Possible Shortness of Breath
No Depression *(Depression = feeling sad)*	0	1	2	3	4	5	6	7	8	9	10	Worst Possible Depression
No Anxiety *(Anxiety = feeling nervous)*	0	1	2	3	4	5	6	7	8	9	10	Worst Possible Anxiety
Best Wellbeing *(Wellbeing = how you feel overall)*	0	1	2	3	4	5	6	7	8	9	10	Worst Possible Wellbeing
No _____ Other Problem *(For example constipation)*	0	1	2	3	4	5	6	7	8	9	10	Worst Possible _____

The next questions concern the general perceptions that you currently have about yourself. Please circle the number that best reflects your current view of yourself using the following scale as a guide for your responses.

		Strongly Disagree	Disagree	Agree	Strongly Agree
1.	On the whole I am satisfied with myself	1	2	3	4
2.	At times I think that I am no good at all	1	2	3	4
3.	I feel that I have a number of good qualities	1	2	3	4
4.	I am able to do things as well as most other people	1	2	3	4
5.	I feel I do not have much to be proud of	1	2	3	4
6.	I certainly feel useless at times	1	2	3	4
7.	I feel that I am a person of worth, at least on an equal plane with others	1	2	3	4
8.	I wish I could have more respect for myself	1	2	3	4
9.	All in all, I am inclined to feel that I am a failure	1	2	3	4
10.	I take a positive attitude toward myself	1	2	3	4

For each question, please **CIRCLE** the number that best describes your sleep habits. Please rate the **CURRENT (i.e. LAST 2 WEEKS) SEVERITY** of your insomnia problem(s).

Insomnia Problem	None	Mild	Moderate	Severe	Very Severe
1. Difficulty falling asleep	0	1	2	3	4
2. Difficulty staying asleep	0	1	2	3	4
3. Problems waking up too early	0	1	2	3	4

4. How **SATISFIED/DISSATISFIED** are you with your **CURRENT** sleep pattern?

Very Satisfied	Satisfied	Moderately Satisfied	Dissatisfied	Very Dissatisfied
0	1	2	3	4

5. How **NOTICEABLE** to others do you think your sleep problem is in terms of impairing the quality of your life?

Not at all Noticeable	A Little	Somewhat	Much	Very Much Noticeable
0	1	2	3	4

6. How **WORRIED/DISTRESSED** are you about your current sleep problem?

Not at all Worried	A Little	Somewhat	Much	Very Much Worried
0	1	2	3	4

7. To what extent do you consider your sleep problem to **INTERFERE** with your daily functioning (e.g. daytime fatigue, mood, ability to function at work/daily chores, concentration, memory, mood, etc.) **CURRENTLY**?

Not at all Interfering	A Little	Somewhat	Much	Very Much Interfering
0	1	2	3	4

For this next question, we would like you to recall the amount of exercise you have done **during the past 12 weeks that was NOT part of the heavy lifting strength training exercise program that you did as part of this study.** This means any exercise you did that was in addition to what you did for this study.

When answering these questions please:

- Only count exercise sessions that lasted 10 minutes or longer in duration.
- Only count exercise that was done during free time (i.e., not occupation or housework).
- Note that the main difference between the first three categories is the intensity of the endurance (aerobic) exercise and the fourth category is for strength (resistance) exercise.
- Write the average frequency on the first line and the average duration on the second.
- Write in "0" if you did not do any exercise in one of the categories.

Considering a **typical week (7-day period) over the past 12 WEEKS,** how many times on average did you do the following kinds of exercise **that was NOT part of the exercise program?** Please write the appropriate number on each line.

AEROBIC EXERCISE	Times Per Week	Average Duration Per Session
a. VIGOROUS EXERCISE = *HEART BEATS RAPIDLY, SWEATING* (e.g., running, aerobics classes, cross country skiing, vigorous swimming, vigorous bicycling)	_____ times/week	_____ minutes/time
b. MODERATE EXERCISE = *NOT EXHAUSTING, LIGHT PERSPIRATION* (e.g., fast walking, tennis, easy bicycling, easy swimming, popular or folk dancing)	_____ times/week	_____ minutes/time
c. LIGHT EXERCISE = *MINIMAL EFFORT, NO PERSPIRATION* (e.g., easy walking, yoga, bowling, shuffleboard)	_____ times/week	_____ minutes/time
RESISTANCE/STRENGTH EXERCISE (e.g., weight lifting, push-ups, sit-ups, resistance band)	_____ times/week	_____ minutes/time

The following questions ask you to rate the exercise program you did **DURING THE PAST 12 WEEKS**. Please pay careful attention to the words and descriptions for each scale and circle the number that best represents how you feel.

1. How beneficial was the exercise program over the past 12 weeks?

1	2	3	4	5
Not at all	A little bit	Somewhat	Quite a bit	Very much

2. How enjoyable was the exercise program over the past 12 weeks?

1	2	3	4	5
Not at all	A little bit	Somewhat	Quite a bit	Very much

3. How supportive were your family/friends of the exercise program over the past 12 weeks?

1	2	3	4	5
Not at all	A little bit	Somewhat	Quite a bit	Very much

4. How motivated were you to do the exercise program over the past 12 weeks?

1	2	3	4	5
Not at all	A little bit	Somewhat	Quite a bit	Very much

5. How difficult was it for you to do the exercise program over the past 12 weeks?

1	2	3	4	5
Not at all	A little bit	Somewhat	Quite a bit	Very much

6. How much control did you have over exercising over the past 12 weeks?

1	2	3	4	5
Not at all	A little bit	Somewhat	Quite a bit	Very much

7. How confident were you that you were able to exercise over the past 12 weeks?

1	2	3	4	5
Not at all	A little bit	Somewhat	Quite a bit	Very much

The next questions ask you about any benefits or harms you feel you experienced from participating in the heavy lifting strength training (HLST) program. Please use the following scales to guide your responses.

-3	-2	-1	0	1	2	3
Very much worse	Somewhat worse	Slightly worse	No change	Slightly better	Somewhat better	Very much better

What effect, if any, do you feel the heavy lifting strength training exercise program had on each of the following for you?

1.	Your physical fitness	-3 (worse)	-2	-1	0	1	2	3 (better)
2.	Your ability to stop thinking about your previous head and neck cancer	-3 (worse)	-2	-1	0	1	2	3 (better)
3.	Your sense of control over your health	-3 (worse)	-2	-1	0	1	2	3 (better)
4.	Your overall muscular strength	-3 (worse)	-2	-1	0	1	2	3 (better)
5.	Your shoulder/neck pain or injury	-3 (worse)	-2	-1	0	1	2	3 (better)
6.	Your shoulder/neck motion	-3 (worse)	-2	-1	0	1	2	3 (better)
7.	Levels of fatigue to carry out other daily activities	-3 (worse)	-2	-1	0	1	2	3 (better)
8.	Your fear of a head and neck cancer recurrence	-3 (worse)	-2	-1	0	1	2	3 (better)
9.	Your overall quality of life	-3 (worse)	-2	-1	0	1	2	3 (better)

Any other positive or negative effects you experienced?

We are also interested in knowing what, if any, barriers you felt made it difficult for you to do the exercise program. Please use the scale below to guide your responses.

1	2	3	4	5	6	7
Not at all		Somewhat		A fair bit		Very much

How much of a barrier was each of the following factors for you in trying to do the heavy lifting strength training exercise program?

1.	Having had head and neck cancer	1	2	3	4	5	6	7
2.	Fear of a cancer recurrence	1	2	3	4	5	6	7
3.	Shoulder/neck pain	1	2	3	4	5	6	7
4.	Muscle/joint injury	1	2	3	4	5	6	7
5.	Bad weather	1	2	3	4	5	6	7
6.	Medical appointments	1	2	3	4	5	6	7
7.	Feeling tired or fatigued	1	2	3	4	5	6	7
8.	Lack of motivation	1	2	3	4	5	6	7
9.	Too busy and had limited time	1	2	3	4	5	6	7
10.	Muscle/joint pain or soreness	1	2	3	4	5	6	7
11.	Feeling sick or not feeling well	1	2	3	4	5	6	7
12.	Travelling to the fitness centre	1	2	3	4	5	6	7
13.	Exercise program was too hard	1	2	3	4	5	6	7

Any other barriers you experienced?

The following questions ask you to rate how you feel about **doing a heavy lifting strength training (HLST) program OVER THE NEXT SIX MONTHS on your own** now that the supervised exercise program is over. Please circle the number that best represents how you feel.

1. How beneficial do you think it will be for you to do a HLST program on your own over the next six months?

1	2	3	4	5
Not at all	A little bit	Somewhat	Quite a bit	Very much

2. How enjoyable do you think it will be for you to do the HLST program on your own over the next six months?

1	2	3	4	5
Not at all	A little bit	Somewhat	Quite a bit	Very much

3. How supportive do you think your family/friends will be if you try to do a HLST program on your own over the next six months?

1	2	3	4	5
Not at all	A little bit	Somewhat	Quite a bit	Very much

4. How motivated are you to do a HLST program on your own over the next six months?

1	2	3	4	5
Not at all	A little bit	Somewhat	Quite a bit	Very much

5. How difficult do you think it will be for you to do a HLST program on your own over the next six months?

1	2	3	4	5
Not at all	A little bit	Somewhat	Quite a bit	Very much

6. How much control do you think you will have over doing a HLST program for the next six months?

1	2	3	4	5
Not at all	A little bit	Somewhat	Quite a bit	Very much

7. How confident are you that you will be able to do a HLST program over the next six months?

1	2	3	4	5
Not at all	A little bit	Somewhat	Quite a bit	Very much

8. Do you have a specific plan for where, when, and how you will do a HLST program on your own over the next six months?

1	2	3	4	5
Not at all	A little bit	Somewhat	Quite a bit	Very much

This important part of the questionnaire is needed to help understand the characteristics of the people participating in the study. All information is held in strict confidence and its presentation to the public will be group data only.

MEDICAL

1. In the past month, was your ability to exercise limited by a health condition, injury, or disability?

1	2	3	4	5
No, Not at All	A Little	Somewhat	Quite a lot	Completely

2. Are you currently taking any medications of health supplements for health problems? (e.g., blood pressure, anxiety, depression, pain, insomnia, etc).

What is the medication? (e.g., beta-blocker, Synthroid)	**What is it for? (e.g., high blood pressure, hypothyroidism)**	**Dose (if known) (e.g., 50mg twice per day; 1 tablet per day)**
1.		
2.		
3.		
4.		
5.		

Participant initials: _____

Questionnaire completion date: __ __ __ __ - __ __ - __ __
y y y y - m m - d d

Please feel free to make any additional comments concerning your head and neck cancer experience, the questionnaire, the exercise intervention, or anything else you think may be helpful to us or think we may have missed.

Appendix E. Consent Form

CONSENT FORM FOR PARTICIPATION IN A RESEARCH STUDY

Feasibility and Safety of Heavy LIFTing Strength Training In Head and Neck Cancer Survivors Post-SurGical Neck Dissection: The LIFTING Trial

(A study to examine the feasibility and safety of a heavy lifting strength training program in head and neck cancer survivors post-neck dissection)

Protocol ID: CC-20-0169

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Sponsor/Funder(s): Canada Research Chairs Program; University of Alberta

Emergency Contact Number (24 hours / 7 days a week): Health Link – *811*

Non-Emergency contact numbers are noted at the end of this document under the section heading 'WHO DO I CONTACT FOR QUESTIONS?". For assistance with terminology within this consent form, please refer to the Canadian Cancer Society Glossary of Terms at http://info.cancer.ca/e/glossary/glossary.html.

You are being invited to participate in a research study because you have been diagnosed with head and neck cancer and have recovered from a surgical neck dissection. This consent form provides detailed information about the study to assist you with making an informed decision. Please read this document carefully and ask any questions you may have. All questions should be answered to your satisfaction before you decide whether to participate.

The study team will tell you about timelines for making your decision. You may find it helpful to discuss the study with family and friends so that you can make the best possible decision within the given timelines.

Taking part in this study is voluntary. You may choose not to take part or, if you choose to participate, you may leave the study at any time without giving a reason. Deciding not to take part or deciding to leave the study will not result in any penalty or any loss of medical or health-related benefits to which you are entitled.

A member of the study team will discuss this study with you and will answer any questions you may have. If you do consent to participate in this study, you will need to sign and date this consent form. You will receive a copy of the signed form.

WHAT IS THE BACKGROUND INFORMATION FOR THIS STUDY?

Head and neck cancers are the sixth most common cancer worldwide, and make up approximately 5%-7% of all solid tumours globally. Incidences of head and neck cancers occur more often in males, with the average age of onset in the 60s. Worldwide, there are 650,000 new cases of HNC, and 350,000 deaths every year, with a five-year overall survival rate of 40%-50%. Standard treatment for early stage HNC is surgery or radiotherapy. Multiple modalities, mainly chemoradiotherapy, are used for locally advanced HNC. Despite improvements in treatments, survivors still endure some physical and psychosocial side effects such as shoulder dysfunction, pain, shortness of breath, weakness, physical fatigue, difficulty sleeping, affected appetite, fear of recurrence, difficulties returning to work, and reduced quality of life.

Strength training has been shown to improve some side effects in HNC survivors but most studies have tested light-to-moderate loads. Although effective, heavy lifting strength training programs may provide additional benefits to head and neck cancer survivors. However, no study using this heavy load training style has been conducted in these survivors.

The Health Research Ethics Board of Alberta – Cancer Committee (HREBA-CC), which oversees the ethical acceptability of research involving humans, has reviewed and granted ethics approval for this study.

WHY IS THIS STUDY BEING DONE?

The purpose of this study is to find out whether or not a heavy lifting strength training program is feasible and safe for you. Additionally, the study will aim to find out what effects this training style has on your strength, physical functioning, quality of life, and psychosocial health.

WHAT ARE OTHER OPTIONS IF I DECIDE NOT TO PARTICIPATE IN THIS STUDY?

You do not have to take part in this study in order to receive continued medical care. Other alternatives in addition to standard care may include:

- starting an exercise program on your own
- consulting with an exercise specialist
- joining a community-based exercise program

Please talk to a member of the study team or your study doctor about the known benefits and risks of these other options before you decide to take part in this study.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

Up to 20 people will take part in this study.

WHAT WILL HAPPEN DURING THIS STUDY?

STUDY INTERVENTION

You will be asked to engage in a heavy lifting strength training exercise program. This program will consist of two supervised exercise sessions per week for 12 weeks. Gradual progressions to lifting heavier loads at higher intensities will take place over a 5 week period. Each exercise session will last approximately one hour, consisting of a warm up, weight training and recovery phases, and cool-down. The duration of the session may be longer or shorter for you than it will be for another person depending on exercise familiarity, how you feel on any given day, and the amount of rest you need between exercises. All supervised exercise sessions will take place in the Behavioural Medicine Fitness Centre at the University of Alberta and will be supervised by a qualified exercise professional and powerlifter.

STUDY PROCEDURES

Established Procedures

The following established procedures will be done as part of this study. Some of these procedures may be done as part of your followup care, in which case the results may be used. Some may be done more frequently than if you were not taking part in this study. Some of these procedures may be done solely for the purpose of the study. If the results show that you are not able to continue participating in the study, the study team will let you know.

- Maximal strength exercise tests: To determine the maximal force that your muscles can exert to overcome the most resistance in one attempt. This test will consist of the barbell squat, deadlift, and bench press. The researchers will monitor your blood pressure and heart rate before and after each session, and will ask you how hard you feel you are working throughout the test. In addition, we will examine how this exercise program affects other outcomes such as muscular strength, fear of cancer recurrence, and quality of life. The test results will also be used to provide an individualized/optimal exercise program based on your fitness at the start of the program.

- Functional fitness tests: To determine your physical function, including strength, flexibility, and agility. Your functional fitness will be assessed through a series of small tests, including walking for 6 minutes, and 30 second sit to stand. Shoulder flexion and abduction ranges of motion will also be measured using a goniometer to assess for the ability to reach overhead. We are trying to determine if the exercise program is effective at improving physical function.

Questionnaires

You will be provided with questionnaires at the following two timepoints: (1) before starting this study (baseline); and (2) at 3 months (post-intervention). The purpose of the questionnaires are to collect information on your demographics, and health behaviours, which will help understand how exercise affects your mental health, quality of life, fatigue, and cancer-related symptoms. Each questionnaire will take about 30-45 minutes to complete.

The information you provide is for research purposes only and will remain strictly confidential. Some of the questions are personal; you may choose not to answer them. Even though you may have provided information on a questionnaire, these responses will not be reviewed by individuals not involved in this study, e.g., your health care practitioner/team. If you would like them to know this information, please bring it to their attention.

	Baseline	*Post-Intervention (3 months)*
Maximal Strength Exercise Tests	*X*	*X*
Functional Fitness Tests	*X*	*X*
Questionnaires	*X*	*X*
Medical Record Review	*X*	*X*

WHAT ARE THE POTENTIAL SIDE EFFECTS FROM PARTICIPATING IN THIS STUDY?

You may experience side effects from participating in this study. Some side effects are known and are listed below, but there may be side effects that are not expected. You should discuss these with the study team.

The study team will watch you closely to see if you have side effects.

Very likely (greater than 21% or more than 20 people in 100):
- It is possible that some people will experience muscle soreness and fatigue following the fitness testing and heavy lifting strength training sessions. This type of response is normal, and will go away after approximately 72 hours. This generally poses no threat to health. If the soreness persists more than five days or might be associated with a muscle or joint injury, participants should contact the study team.

Rarely (1 – 4% or less than 5 in 100 people):
- During and immediately after the strength test, it is possible to experience symptoms such as abnormal blood pressure, fainting, light-headedness, muscle cramps or strain, nausea, and in very rare cases (1 per 20,000 in testing facilities) heart rhythm disturbances or heart attack. While serious

risk is highly unlikely, such risks must be acknowledged, and participants must willingly assume the risks associated with exercise.

WHAT ARE THE BENEFITS OF PARTICIPATING IN THIS STUDY?

Participation in this study may or may not be of personal benefit to you.

Based on the results of this study, it is hoped that, in the long-term, patient care can be improved.

WHAT ARE MY RESPONSIBILITIES AS A STUDY PARTICIPANT?

If you choose to participate in this study, you will be expected to:

- Tell the study team about your current medical conditions;
- Tell the study team about all prescription and non-prescription medications and supplements, including vitamins and herbals, that you may be taking and check with the study team before starting, stopping or changing any of these. This is for your safety as these may interact with the intervention you receive on this study;
- Tell the study team if you are thinking about participating in another research study;
- Attend all scheduled study visits and undergo all of the procedures described above;
- Return any questionnaires taken home to complete;
- Follow your supervised exercise sessions for 12 weeks.

HOW LONG WILL I BE PARTICIPATING IN THIS STUDY?

The study intervention will last for about 12 weeks and you will also be asked to complete questionnaires before and after the exercise intervention.

You will be asked to come to one of our testing locations (Cross Cancer Institute or University of Alberta) for fitness and functioning tests before starting this study and then be asked to come back to one of our testing locations to complete assessments after 12 weeks. Questionnaires will also be completed before starting the study and after 12 weeks.

CAN I CHOOSE TO LEAVE THIS STUDY EARLY?

You can choose to end your participation in this research (called early withdrawal) at any time without having to provide a reason. If you choose to withdraw early from the study without finishing the intervention, procedure or follow-up, you are encouraged to contact the study doctor or a member of the study team.

If you decide to leave the study, you can ask that the information that was collected about you not be used for the study. Let the study team know if you choose this.

CAN MY PARTICIPATION IN THIS STUDY END EARLY?

The study team may stop your participation in the study early, and without your consent, for reasons such as:

- They believe it is in your best interest to do so;
- You are unable to complete the required study procedures;
- You do not follow the study rules;
- The research ethics board withdraws permission for the study to continue;

If this happens, it may mean that you would not receive the study intervention for the full period described in this consent form.

If you are removed from the study, the study team will discuss the reasons with you and plans will be made for your continued care outside of the study.

HOW WILL MY PERSONAL INFORMATION BE KEPT CONFIDENTIAL?

If you decide to participate in this study, the study team will only collect the information they need for this study.

Records identifying you, including information collected from your medical files/records, such as your Electronic Medical Records (EMR), Netcare, charts, etc., will be kept confidential to the extent permitted by the applicable laws, will not be disclosed or made publicly available, except as described in this consent document.

Authorized representatives of the following organizations may look at your identifiable medical/clinical study records at the site where these records are held for quality assurance purposes and/or to verify that the information collected for the study is correct and follows proper laws and guidelines:

- University of Alberta
- Alberta Health Services
- The Health Research Ethics Board of Alberta – Cancer Committee, which oversees the ethical conduct of this study;

Authorized representatives of the above organizations may **receive** information related to the study from your medical/clinical study records that will be kept confidential in a secure location and may be used in current or future relevant health research. Your name or other information that may identify you will not be provided (i.e., the information will be de-identified). The records received by these organizations will be coded with a number. The key that indicates what number you have been assigned will be kept secure by the researchers directly involved with your study and will not be released.

Any disclosure of your identifiable health information will be done in accordance with federal and provincial laws including the Alberta Health Information Act (HIA). The organizations listed above are required to have organizational policies and procedures to protect the information they see or receive about you, except where disclosure may be required by law. The study team will ensure that any personal health information collected for this study is kept in a secure and confidential location (Behavioural Medicine Laboratory, University of Alberta) as also required by law.

If the results of this study are published, your identity will remain confidential. It is expected that the information collected during the study will be used in analyses and will be published/presented to the scientific community at meetings and in journals.

Even though the likelihood that someone may identify you from the study data is very small, it can never be completely eliminated. Every effort will be made to keep your identifiable information confidential, and to follow the ethical and legal rules about collecting, using and disclosing this information.

Studies involving humans sometimes collect information on race and ethnicity as well as other characteristics of individuals because these characteristics may influence how people respond to different interventions. Providing information on your race or ethnic origin is voluntary.

A copy of the consent form that you sign to enter the study will be included in your health record/hospital chart.

WILL MY HEALTHCARE PROVIDER(S) BE INFORMED OF MY PARTICIPATION IN THIS STUDY?

Your family doctor/health care provider may be informed that you are taking part in a study so that you can be provided with appropriate medical care. If you do not want your family doctor/health care provider to be informed, please discuss with your study team to find out your options.

WILL THERE BE ANY COSTS INVOLVED WITH PARTICIPATING IN THIS STUDY?

Participation in this study will not involve any additional costs to you or your private health care insurance. The study team will cover all study-related costs including fitness testing, exercise supervision, and parking for study-related visits.

WILL I BE COMPENSATED FOR PARTICIPATING IN THIS STUDY?

You will not be paid for taking part in this study.

If you decide to participate in this study, you will be reimbursed for study-related expenses such as parking or public transportation.

WHAT ARE MY RIGHTS AS A PARTICIPANT IN THIS STUDY?

You will be told, in a timely manner, about new information that may be relevant to your willingness to stay in this study.

You have the right to be informed of the results of this study once the entire study is complete. If you would like to be informed of these results, please contact the study team.

The results of this study will be available on a clinical registry; refer to the section titled “Where can I find online information about this study?”.

Your rights to privacy are legally protected by federal and provincial laws that require safeguards to ensure that your privacy is respected.

By signing this form you do not give up any of your legal rights against the hospital, investigators, sponsor, involved institutions for compensation or their agents, nor does this form relieve these parties from their legal and professional responsibilities.

IS THERE CONFLICT OF INTEREST RELATED TO THIS STUDY?

There are no conflicts of interest related to this study.

WHERE CAN I FIND ONLINE INFORMATION ABOUT THIS STUDY?

A description of this clinical trial will be available on http://www.clinicaltrials.gov. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search for this website at any time.

The study registration number to use this website is: NCT04554667

WHO DO I CONTACT FOR QUESTIONS?

If you have questions about taking part in this study, or if you suffer a research-related injury, you should talk to the study team, co-investigator or study coordinator. These person(s) are:

Name	Telephone
Kerry Courneya (Principal Investigator)	780-492-1031
Margaret McNeely (Co-Investigator)	780-248-1531
Hadi Seikaly (Co-Investigator)	780-407-3691
Daniel O'Connell (Co-Investigator)	780-407-7250
Stephanie Ntoukas (Study Coordinator)	780-492-2829

A wallet card will be provided to you with information about how to contact the study team when required.

If you have questions about your rights as a participant or about ethical issues related to this study and you would like to talk to someone who is not involved in the conduct of the study, please contact the Office of the Health Research Ethics Board of Alberta – Cancer Committee (HREBA-CC) at:

Telephone: 780-423-5727 Toll Free: 1-877-423-5727

SIGNATURES

Part 1 - to be completed by the potential participant.

	Yes	No
Do you understand that you have been asked to take part in a research study?	☐	☐
Do you understand why this study is being done?	☐	☐
Do you understand the potential benefits and risks of taking part in this study?	☐	☐
Do you understand what you will be asked to do should you decide to take part in this study?	☐	☐
Do you understand the alternatives to participating in this study?	☐	☐
Do you understand that you are free to leave the study at any time, without having to give reason and without affecting your future health care?	☐	☐
Do you understand who will see your records, including health information that identifies you?	☐	☐
Do you understand that by signing this consent form you are giving us permission to access your health information and specimens if applicable?	☐	☐
Do you understand that by signing this consent form that you do not give up any of your legal rights?	☐	☐
Do you understand that your family doctor/health care provider will/may be informed of your participation in this study?	☐	☐
Have you had enough opportunity to ask questions and discuss this study?	☐	☐

By signing this form I agree to participate in this study.

_____	_____	_____
Signature of Participant	PRINTED NAME	Date

Part 2 - to be completed by the study doctor or designee who conducted the informed consent discussion. Only complete this section if the potential participant has **agreed** to participate.

I believe that the person signing this form understands what is involved in the study and has freely decided to participate.

Signature of Person Conducting the Consent Discussion	PRINTED NAME	Date

Part 3 - to be completed only if the participant is unable to read or requires assistance of an oral translator/interpreter.

- The informed consent form was accurately explained to, and apparently understood by the participant.
- Informed consent was freely given by the participant.

Signature of Impartial Witness/Interpreter	PRINTED NAME	Date

You will be given a copy of this signed and dated consent form prior to participating in this study.