1.0 Title of Research Project:

Pilot Study on Nordic Pole Walking and Individuals with Non-Small Cell Lung Cancer: Effects on Physical Function and Quality of Life

2.0 Rationale: Statement of Need

Research has shown that patients fear disability more than other complications that result from Non-Small Cell Lung Cancer (NSCLC) or its treatments(1). Lung cancer patients experience a high symptom burden including dyspnea, cough, fatigue, and pain(2). Patients also struggle with sleep disturbances, anxiety, depression and fear as well as reporting impaired quality of life(3). Upon diagnosis patients with NSCLC have decreased physical activity levels and over time a continuing cycle of inactivity and functional decline as strength and cardiovascular fitness deteriorates with worsening symptoms(4, 5). As a result, exercise is being recognized for its potential to improve overall function in addition to increased longevity in this population(6, 7).

The benefits of exercise training have been well documented in other chronic respiratory disease populations such as individuals with chronic obstructive pulmonary disease or interstitial lung disease (8, 9) and may also benefit the NSCLC population. Studies have shown exercise interventions are safe, feasible and well tolerated by patients with NSCLC (10-12), but further research is needed to understand the effectiveness of specific exercise interventions (12, 13). There is also a need for further exploration of outcomes such as health related quality of life (HRQoL), fatigue, pain, dyspnea and fear of recurrence. Furthermore, there remains a lack of knowledge regarding the sustainability and long-term effects of exercise on this population (12). This knowledge would help to guide clinicians and policymakers in their efforts to improve quality of life in this patient population.

3.0 Background and Literature:

3.1 Epidemiology of Lung Cancer in Canada: In 2014 it is estimated that 26,100 people in Canada were newly diagnosed with lung cancer(14). This accounts for about 13.6% of all new cancer diagnoses(14). Lung cancer is the leading cause of cancer related deaths in Canada. About 20,500 people were expected to die of lung cancer in 2014: more than breast, prostate and colorectal cancers combined(14). Cancer is considered to be the third most costly disease after cardiovascular and musculoskeletal diseases(15); cancer care in Canada was estimated to cost $14.2 billion in 1998(15). A study published in 2013 looking at cancer costs in Ontario reviewed the costs of 402,399 patients who were 19 years of age and older and had been diagnosed with different cancers(15). It was determined that the overall mean cost per lung cancer patient during the first year post-diagnosis was $31,550 (2009 Canadian dollars)(15). This study also found that lung cancer (together with colorectal breast and prostate cancers) presented the largest financial burden to the Ontario health care system with hospital admissions being the greatest contributor to these high costs(15). Other resource categories that contributed significantly to the cost were chemotherapy, physician services and diagnostic testing(15).

3.2 Pathophysiology of Lung Cancer: Lung cancer is a malignant tumour that originates in the cells of the lungs(16). Individuals who have been exposed to tobacco smoke, asbestos and radiation are at increased risk of developing lung cancer(16). Ninety percent of people diagnosed with lung cancer are asymptomatic and hemoptysis (the coughing up of blood) is the most common

first sign(16).

Lung cancer is classified as either small cell lung cancer or NSCLC. Small cell lung cancer originates in the bronchi in the centre of the lung and is the most aggressive of all types of lung cancer, usually resulting in metastases to other parts of the body(16). It comprises approximately 10 to 15% of all lung cancer cases(16).

NSCLC is the most common type of lung cancer accounting for 85 to 90% of all cases(16). There are three main types of NSCLC: 1) adenocarcinoma (usually begins in the periphery of the lung), 2) squamous cell carcinoma (almost always found in people with a history of smoking and is usually located in the large bronchi near the centre of the lung), and 3) large cell carcinoma (least common type of NSCLC)(16). The earlier NSCLC is diagnosed and treated the better the prognosis(16). Upon diagnosis NSCLC is classified based on the extent of cancer in the body using the "tumour, nodes, metastasis" (TNM) system(16). This system outlines the size of the primary tumour, the number and location of any regional lymph nodes that have cancer cells in them, and whether the cancer has metastasized to another part of the body(16). There are four stages in the TNM classification system and the first three stages are divided into A and B subgroups where the prognosis of B is progressively worse than A(16). The following descriptions of each stage can be applied to most NSCLC diagnosis: i) *Stage I:* Tumours are less than 3 cm in diameter and are completely within the lung. ii) *Stage II:* Tumours have metastasized to the bronchial or hilar lymph nodes. iii) *Stage III:* Tumours have metastasized to the mediastinal lymph nodes. iv) *Stage IV:* Tumours have metastasized to the pleura, the other lung or to other organs outside of the chest(16).

Depending on the stage of cancer, health history and functional ability treatments for NSCLC include lung resection, chemotherapy, radiation therapy or a combination thereof(16). The survival rate of those diagnosed with NSCLC is considerably better than those diagnosed with small cell lung cancer. Forty percent of NSCLC patients who undergo complete lung resection of the primary tumour survive up to five years(16). For those diagnosed with small cell lung cancer, lung resection is rarely an option and median survival rates range from 313 to 388 days(16). This research project will include patients who have been diagnosed with NSCLC because of its higher prevalence and survival rate.

3.3 Exercise & Lung Cancer: Exercise interventions for NSCLC patients pre- and post-surgery have been determined safe, feasible and well tolerated, even in those with advanced and metastatic disease (10-12). Additionally, low to moderate intensity exercise was found to be well tolerated in patients with NSCLC who underwent chemotherapy and/or radiation treatment (17, 18). Recent reviews of physical activity and exercise in lung cancer report that exercise has been shown to reduce symptoms, increase exercise tolerance, improve quality of life and potentially reduced length of stay and post-operative complications(19, 20). To better understand exercise as applied to NSCLC patients there is a need to generalize according to the specific populations that are studied (perioperative and advanced disease).

1) *Perioperative Exercise:* In 2013 a Cochrane review identified three RCTs involving 178 participants who had participated in an exercise intervention within 12 months of lung resection for NSCLC(13). The review reported that exercise capacity as measured by the six-minute walk test (6MWT) as greater in the intervention group compared to the control group (mean difference (MD) 50.4m; 95% confidence interval (CI) 15.4 to 85.2m)(13). There was no reported difference in HRQoL between groups (standardized mean difference (SMD) 0.17; 95% CI -0.16 to 0.49)(13). Authors noted that the results of this review should be interpreted with caution due to significant risks of bias and small sample sizes(13). Only one of the studies described blinding of outcome assessors and all of the studies were found to have evidence of performance bias(13). The quality of evidence in this research area is

negatively affected by the limited number of RCTs that have been done(13).

Three systematic reviews investigated the effect of exercise in the NSCLC population. Granger et al. (2011) systematically reviewed the literature (n=675, 2 RCTs, 8 prospective case series, a retrospective case series, a prospective cohort trial and a retrospective cohort trial)(21). Interventions included aerobic training, resistance training, stretching exercises or a combination thereof and outcomes included exercise capacity, HRQoL and safety (21). Overall NSCLC patients benefited from exercise interventions pre-operatively or post-cancer treatment including surgery, chemotherapy and radiation treatment as exercise capacity, symptoms were found to improve(21). General HRQoL was also affected(21). Exercise was also found to be safe for NSCLC patients before and after cancer treatment(21).

Crandall et al. (2014) systematically reviewed the literature (n=575, 8 RCTs, 10 single group trials) on exercise interventions for lung cancer patients who were surgically treated(12). Studies included in this review involved exercise interventions that were supervised or unsupervised inpatient, outpatient, community or home-based(12). Researchers concluded that exercise led to improved cardiopulmonary exercise capacity, increased muscle strength and reduced fatigue, post-operative complications and hospital length of stay in patients with resectable NSCLC(12). Three RCT's measured the effects of post-operative exercise programs on HRQoL and found no significant difference between groups. However, differences in HRQoL measurement tools (generic/specific), intervention designs and the extent of surgery made comparison between studies difficult(12). Future studies need to use equal measurement tools that have been proven to be reliable and valid within the specific patient population(12).

Rodriguez-Larrad et al. (2014) conducted a systematic review (n=599, all 8 studies were RCTs) examining the use of perioperative respiratory physiotherapy in patients who underwent pulmonary resection for lung cancer(22). Some study interventions included chest physiotherapy or intermittent positive pressure breathing only while others also involved aerobic and resistance training(22). Each study included in the review examined at least two or more of the following outcome variables: functional capacity, postoperative pulmonary complications (PPC) or prolonged length of hospital stay (LOS)(22). Pre-operative aerobic exercise in patients undergoing lung cancer resection was found to improve functional capacity and reducing postoperative morbidity(22). The addition of aerobic and resistance training to the usual care or standard physiotherapy in the post-operative period did not reduce PPC or LOS in patients undergoing lung resection(22). These results should be taken with caution because of the high variability in the types of interventions used; it is not possible to establish the effectiveness of each individual intervention(22).

To summarize, evidence indicates that perioperative exercise is safe and that exercise may benefit the exercise capacity and HRQoL of lung cancer patients. Due to significant between-study heterogeneity within the systematic reviews, it was inappropriate to conduct meta-analyses and pool results(12, 21, 22). Future research should continue to analyze various types of exercise in order to inform the optimum exercise prescription and setting for NSCLC patients. In addition larger sample sizes, clear reporting structure and adequate allocation concealment should also be considered.

2) *Advanced Disease:* Patients with advanced stages (IIIA, IIIB, IV) of NSCLC have notably decreased exercise capacity. Yilmaz et al (2013) determined this to be a result of decreased pulmonary function and peripheral muscle strength(4). In addition reduced exercise capacity negatively impacts functional categories of HRQoL in these patients(4). Holland et al.

(2013), believed that the combination of symptoms, including diminished muscle strength, decreased HRQoL, increased dyspnea and greater levels of fatigue provide a strong rationale for referring this patient population to a pulmonary rehabilitation program(23).

In 2013 Cheville et al. in a RCT (n=66) examined the effects of a home-based walking and strength training exercise program (versus usual care) on function, fatigue and sleep quality in patients with stage IV lung and colorectal cancer(24). Twenty out of 26 of the participants in the intervention group adhered to the program. They showed improvement in mobility (p=0.01), fatigue (p=0.02) and sleep quality (p=0.05) over time. The mean changes (from baseline to week eight) between the intervention and control groups in mobility (p=0.002), fatigue (p=0.03), and sleep quality (p=0.002) also significantly differed. (24). Henke et al. (2014) also conducted a RCT (n=46) to test the effects of strength and endurance training on the independence and quality of life in lung cancer patients with advanced disease during three cycles of palliative chemotherapy treatment(25). The intervention group (n=18) participated in cardiovascular exercise daily and strength training every other day(25); the control group (n=11) received conventional physiotherapy consisting of manual therapy and breathing techniques(25). Out of 46 patients only 29 completed the trial; 17 patients ended the trial early due to death (n=6), non-compliance (n=10) or because they continued treatment at a different hospital (n=1)(25). A significant difference between groups was found in physical function, self-reported symptoms (pain, neuropathy, cognitive functioning, dyspnea) and exercise capacity(25).

This evidence suggests that exercise capacity and symptom burden in patients with advanced lung cancer can be improved with exercise, however frequency, duration and intensity of prescription are not certain. Most studies on exercise in this population have consisted of in-hospital supervised exercise programs, which may be restrictive to some patients and has been associated with poor compliance. There is a need to further examine home-based exercise programs including new modalities of exercise that may not have been accessible in the clinical setting(26).

3.4 Nordic pole walking: Nordic pole walking (NPW) is a low-impact form of exercise that involves walking with a pair of poles customized to the participant's height and stride length. While NPW has become an increasingly popular type of exercise, little research has been done to determine the effects of NPW on the cancer population let alone the NSCLC patient population. Tschentscher et al. (2013) conducted a systematic review to summarize and interpret the health benefits of NPW and to compare the effects of NPW to brisk walking and jogging on heart rate, maximal oxygen consumption (VO_2max), HRQoL and other health measurements in healthy and chronic disease populations(27). Included in this review were 16 RCTs (n=1062) and 11 observation studies (n=831)(27). Two RCTs on healthy subjects were included in the review(28, 29). Kukkonen-Harjula et al. (2007) conducted an RCT (n=121) investigating the effects of a self-guided 12-week (40 minutes, 4 times per week) program involving NPW (n=60) and walking (n=61) on health-related fitness in 50-60 year old sedentary women(29). Improvement was recorded in maximum heart rate, respiratory exchange ratio, VO_2max, and lactate threshold, but there was no between group difference found(29). The second RCT (n=168) by Hagner et al. (2009) examined the physiological effects of premenopausal (n=65), perimenopausal (n=53), and postmenopausal (n=53) women participating in a twelve week NPW program that consisted of three 90-minutes sessions of NPW per week(28). For all of the groups studied there was a significant increase in VO_2max and high-density lipoprotein (HDL) and a reduction in total cholesterol, low-density lipoprotein (LDL), triglycerides and BMI ($p<0.01$)(28) over time. No group differences were reported and there was no control group. These results demonstrated that NPW combined with an effort to

maintain a healthy diet significantly influences the well being of premenopausal, perimenopausal and postmenopausal women over time (28). Several observational studies have supported the results of these two RCTs by showing similar short-term effects of NPW in the healthy population including increased VO_2, higher peak heart rate, raised respiratory exchanged ratio and higher energy expenditure than brisk walking at the same pace(30-32).

Tschentscher et al. also looked at the effects of NPW on different chronic disease populations including those with COPD(33) and breast cancer(34). A RCT (n=60) conducted by Breyer et al. (2010) measured the short- and long-term effects of NPW on COPD patients' daily physical activity levels and exercise capacity. The NPW group (n=30) trained for 60-minutes three times per week at an intensity of 75% of maximum heart rate, compared to the sedentary control group (no poles or exercise) (n=30). Daily physical activity and the 6MWT increased with NPW (both $p<0.01$). Furthermore, NPW decreased exercise-induced dyspnea (Borg dyspnea score) and anxiety and depression (Hospital Anxiety and Depression Scale) and improved HRQoL (SF-36 Physical Component Summary and Mental Component Summary; all $p<0.01$). There were no changes in lung function parameters or medication use. In addition another research study by Barberan-Garcia et al. (2015) (cross-sectional design; n=16) compared the physiological response during NPW on solid ground and beach sand to regular walking in the COPD population(35). NPW on solid ground and beach sand resulted in higher VO_2 plateaus compared with the 6MWT (no poles) and peak VO_2 during the incremental shuttle test ($p<0.05$ each)(35). There was no difference in rate of perceived exertion (RPE) observed between NPW on solid ground compared to the 6MWT and the incremental shuttle test, however RPE during NPW on beach sand was significantly higher than all other exercise protocols ($p<0.05$)(35). This study showed that NPW could generate higher VO_2 compared to regular walking in COPD patients with little influence on dyspnea. Therefore it might be a suitable way to enhance community-based training programs in COPD patients(35).

Sprod et al. (2005) completed an RCT (n=12) to compare the effects of an 8-week NPW exercise program on shoulder range of motion (ROM) and upper body muscular endurance in breast cancer survivors(34). The intervention group (n=6) participated in 20-minutes of NPW outdoors twice per week, while the control group (n=6) walked outdoors without poles twice per week(36). As part of the program both groups performed 30-minutes of resistance training and concluded with stretching exercises(36). The intervention group demonstrated significant improvement ($p<0.05$) in upper body muscular endurance on bench press and lat pull down exercises over the 8-week study, while the control group showed no significant change over the same time period(36). The between group differences were not reported. This study indicates that for breast cancer survivors NPW is more beneficial than regular walking as it results in an improved muscular endurance of the shoulder muscles(34).

In summary, the research above suggests that the short-term and long-term effects of NPW are beneficial to both the healthy population and those with COPD and breast cancer. However, due to small sample sizes and poor methodological quality caution should be used when drawing conclusions from these studies.

3.5 <u>The Pilot Study:</u> Pilot studies are conducted to assess feasibility prior to conducting a large-scale investigation(37). They are an important step in the research process. The purpose of running a pilot study is usually related to trialing a study design and/or testing a new instrument and establishing that investigators understand the research protocol and are able to collect data in a consistent manner(38). Specific rationale for performing a pilot study can be classified into four categories: i) *Process:* To assess operational processes that take place within the study(37). For example, determining recruitment rates and retention rates. ii) *Resources:* To assess any difficulties that may occur related to time and budget(37). For example, the length of time it

takes for participants to complete questionnaires. iii) *Management:* To observe any potential human and data optimization problems that may occur(37). For example, issues that may arise at participating centres. iv) *Scientific:* To assess treatment safety, determine dose levels and response and estimate treatment effect and its variance(37). While pilot studies have little to contribute statistically and theoretically, they provide extensive understanding of the research process(38). Therefore, researchers need to remain open-minded, using the results of the pilot study to adapt the design and operational processes of a full study(38).

3.6 Knowledge Gaps and Contribution to Research: There is a growing body of evidence supporting exercise in the NSCLC population and health care professionals are encouraged to recommend that NSCLC patients participate in an exercise program. However, there is a need to establish the most appropriate and effective exercise prescription for this population. Currently, there is insufficient evidence regarding the optimal exercise type and prescription for the NSCLC population(12). To assist health care professionals with making exercise recommendations for this population more rigorous, methodological studies (i.e. RCTs) examining the effects of various exercise types and prescriptions, such as resistance training and Nordic pole walking are needed. To accomplish this a feasibility or pilot study is required to establish the optimal study design, population, assessment tools, interventions and operational processes. It has been recognized that poor accessibility to rehabilitation programs for lung cancer patients is a barrier to exercise program participation (ref Didier). Therefore future studies should consider home-based programs particularly for those with advanced disease.

NPW has been selected as an appropriate exercise for NSCLC patients because of its ability to be a more intense and beneficial exercise compared to regular walking(27). It also allows patients to exercise independently. A study of individual/group exercise using NPW will be the first of its kind and is the first step to establishing the appropriate NPW exercise prescription including the optimal frequency, intensity and time spent NPW for individuals with NSCLC.

4.0 Research Objectives, Questions & Hypotheses

The *primary research question* is*:* 1) What is the optimal design (patient sample, instruments) and operational processes to assess the effects of NPW on individuals who have been diagnosed with stage I-IV NSCLC? *Secondary research questions* are: 2) How does participating in an eight-week Nordic pole walking program affect physical function, and 3) health related quality of life (HRQoL) of these individuals?

The *primary objective* is to assess the feasibility of a NPW program for individuals with stage I-IV NSCLC by establishing the optimal design and operational processes. The *secondary objectives* are to: determine the effects of NPW on 1) physical function, and 2) HRQoL.

Hypotheses are that the NPW program for individuals who have been diagnosed with stage I-IV NSCLC will: 1) be feasible; 2) improve physical function; and 3) improve the HRQoL.

5.0 Methods:

5.1 Study Design: This is an eight-week multi-centre randomized controlled pilot study to establish optimal study design and operational processes to inform a larger scale study(37, 38). The intervention group will participate in an individualized NPW program, while the control group continues their usual daily routine. The control group is necessary because it increases the reliability of the results by allowing researchers to compare the control group measurements to the intervention group measurements.

5.2 Location of Research:

1. Lakeridge Health, Oshawa, Ontario (n=5 intervention, n=5 control, approximate eligible population at Lakeridge is 300, this is based on current and new cases of lung cancer at the Durham Regional Cancer Centre)
2. Southlake Regional Health Centre, Newmarket, Ontario (n=5 intervention, n=5 control)
3. Abilities Centre, Whitby, Ontario (ATTACHMENT 1)
4. Magna Centre, Newmarket, Ontario (ATTACHMENT 2)

5.3 Sample Selection: The *inclusion criteria*: 1) primary diagnosis of histologically confirmed stage I-IV NSCLC (with any concurrent cancer treatment), 2) approval of primary treating physician, and 3) ≥ 18 years old. The *exclusion criteria*: 1) not able to communicate in English, 2) unable to consent, e.g. incapable, and 3) use of Nordic walking poles on a regular basis within the last six months. We will presume the study participant is capable with respect to the research study unless we suspect incapacity exists based on: the physician's assessment; direct observation of the person e.g., the person is confused, disoriented, depressed, psychotic, extremely anxious, unable to make a decision, intoxicated; or from information obtained from family or other caregivers.

5.4 Recruitment: We anticipate recruiting a minimum of 20 individuals with NSCLC (n=10 intervention group, n=10 control group). It is important that the pilot study be representative of the target study population(37, 38). The sample size needs to be large enough to provide useful information about the feasibility of the study(37, 38). Recruitment and enrolment will take place from approximately November 2015 – April 2016. The recruitment procedures are as follows:

1) Lakeridge Health: Potential study participants will be screened (ATTACHMENT 3) and introduced to the study by the primary treating physician (upon approval) and/or the staff (oncology nurses) during their clinical visits. These physicians and nurses are not investigators or paid personnel in the study. Potential participants will be provided with a study information page (ATTACHMENT 4) by the physicians or nurses to read at their own pace. Interested potential participants will be asked to contact the researchers about the study. Upon being contacted a research team member will explain the study and obtain verbal consent (ATTACHMENT6) over the telephone. Written consent (ATTACHMENT 5) will be provided during the first face-to-face visit at the recreation centre.

2) Southlake Regional Health Centre: Potential study participants will be screened (ATTACHMENT 7) and introduced to the study by the primary treating physician (upon approval) and the staff (oncology nurses) during their clinical visits. These physicians and nurses are not investigators or paid personnel in the study. Potential participants will be provided with an study information page (ATTACHMENT 4) by the physicians or nurses to read at their own pace. Interested potential participants will provide consent to the nurses to release their contact information to the research team. The name and contact information of participants will then be forwarded to the research team. Upon receipt of this information a research team member will explain the study and obtain verbal consent (ATTACHMENT6) over the telephone. Written consent (ATTACHMENT 5) will be provided during the first face-to-face visit at the recreation centre.

3) Posters (ATTACHMENT 8) informing potential participants about the study will be displayed at Lakeridge Health, Southlake Health Centre and various community based cancer centres (eg. Wellspring Cancer Centre). If participants are interested they will be asked to contact the research team using the information on the poster, who will then explain the study and obtain verbal consent (ATTACHMENT 6) over the telephone. Participants will be asked to discuss the study with and obtain approval from their primary

treating physician at their next follow-up appointment. Written consent (ATTACHMENT 5) will be provided during the first face-to-face visit at the recreation centre.

4) *NPW Information Sessions* will be held at the recreation facilities where the NPW program will take place (Abilities Centre & Magna Centre). The purpose of these information sessions is to allow potential participants the opportunity to learn more about NPW including the risks and benefits of participating in this activity. Research team members will demonstrate NPW, explain the study and answer any questions that potential participants may have. Any potential participants who are interested will then speak on an individual basis with research team member who will then thoroughly explain the study and obtain written consent (ATTACHMENT 5). Pariticipants will be asked to obtain approval from their primary treating physician at their next follow-up appointment.

5) *Other strategies:* We expect the strategies above (especially the first two) will be our primary recruitment techniques. If we are experiencing problems with recruitment we will use a variety of other strategies to identify and recruit potential participants including: snowball referrals from clinician experts, professional societies (e.g., Respiratory Therapy Society of Ontario), and patient advocacy groups (e.g., Ontario Lung Association) and via social media specifically Twitter and Facebook (ATTACHMENT 34). Twitter is a successful tool not only for disseminating research findings but also for planning studies and recruiting participants (e.g. the research of Marina Bastawrous @mbastaw).

5.5 Outcomes:

5.5.1 *Feasibility:* The feasibility objectives for this pilot study are to:

1. verify recruitment, consent and randomisation procedures;
2. confirm the sample size required for a fully study;
3. confirm the inclusion/exclusion process;
4. test the appropriateness of assessment tools used in the study;
5. determine appropriate timing of data collection;
6. confirm that the data collection materials are sufficient;
7. monitor the operational processes; and
8. formalize the protocols for Nordic pole walking exercise prescription.

See the chart in ATTACHMENT 9 for further explanations and a more detailed list of feasibility measurements. Notes regarding the study process will be documented throughout the study. Participants upon study completion will also complete a program evaluation survey (ATTACHMENT 10) to reflect on their experience.

5.5.2 *Participant Characteristics:* Participant demographics (ATTACHMENT 11), general health history, smoking status, physical activity level (ATTACHMENT 12)(39), height, weight, girth measurements (bicep, chest, waist, hips and thigh), resting heart rate and oxygen saturation levels (ATTACHMENT 13) will be recorded to provide further understanding of the composition of the participant group.

5.5.3 *Physical Function:*

1) *Lower body physical function* will be measured using the 6MWT(40) and the 30-second (30-s) chair stand test(41). The 6MWT has been recognized by the American Thoracic Society as a valid measure of submaximal functional capacity in those with pulmonary disease(40). This self-paced test measures the distance that an individual can walk over a 25 or 30m track in six minutes(40). Granger et al. estimated the minimal important difference for

deterioration of the 6MWT in lung cancer to be between 22m and 42m or a change of 9.5%(42). Having a greater 6MWT distance was correlated with better function, increased physical activity and decreased dyspnea(42). The 30-s chair stand test is a valid indication of lower body strength in the older adult population(41). The test requires participants to complete as many sit to stands as possible in 30 seconds(41). The 30-s chair stand test has been used to assess lower body strength in pulmonary fibrosis patients(43) and the COPD population(44).

2) *Upper body physical function* will be assessed with the unsupported upper limb exercise test (UULEX)(45, 46) and the handgrip strength test. The UULEX is a valid incremental test that has been used to measure peak unsupported arm exercise capacity in the chronic lung disease population (45, 46). The test requires the seated participant to lift a plastic bar (0.2kg) through eight levels at a constant cadence of 30 beats per minute as directed by a metronome. Once the maximum height is reached the weight of the bar is increased by 0.5kg every minute to a maximum weight of 2.0 kg. The test continues until the participant experiences fatigue and decides to stop. The results are recorded in seconds. Handgrip strength is correlated with survival, weight loss, sarcopenia and quality of life characteristics in advanced cancer patients(47, 48). As recommended by the American Society of Hand Therapists grip strength will be measured using a dynamometer with the handle in the second position. Individuals will be seated with their shoulder adducted and elbow flexed 90º and their forearm in neutral. Three successive trials for both hands will be recorded.

5.5.4 *HRQoL:* HRQoL has been shown to be a significant independent predictor of survival duration in the cancer population(49). We will assess HRQoL in NSCLC patients using the SF-36 (ATTACHMENT 14)(50) and the Functional Assessment of Cancer Therapy – Lung (FACT-L) (version 3) (ATTACHMENT 15)(51).

The SF-36 has been validated and used extensively as a measure of HRQoL(50). It assesses eight health concepts: 1) Limitations in physical activities because of health problems; 2) Limitations in social activities because of health problems; 3) Limitations in usual role activities because of health problems; 4) bodily pain; 5) general mental health (psychological distress and well-being); 6) limitations in usual role activity because of emotional problems; 7) vitality (energy and fatigue); 8) general health perceptions. The SF-36 has been used in other studies to examine HRQoL in the NSCLC population(52-55).

The FACT-L is a 44-item self-report instrument that measures quality of life using the following dimensions: physical well-being, emotional well-being, social well-being, functional well-being and disease specific concerns(51). The questionnaire begins with the FACT- General (FACT-G); a HRQoL questionnaire that was developed to be used with patients who have any form of cancer(51). It is supplemented with the Lung Cancer Subscale (LCS), which was designed to complement the FACT-G by obtaining related information about the symptom experience of people with lung cancer(51). The FACT-L has been proven to be reliable, valid, and sensitive to change in performance status(51).

6.0 Study Procedures (For a detailed flow diagram of study procedures see ATTACHMENT 16.)

6.1.1 Randomization: Randomization of intervention and control groups will be computer generated(56) and administered by the research development assistant at the university, Danielle Dawson. Danielle will be kept at arm's length from the study to mitigate the risk of bias for the random allocation. Allocation will be concealed by placing the assignment within aluminum foil, and then in opaque envelopes. Study participants will choose and open the allocation envelope.

6.1.2 Assessment: Written consent (ATTACHMENT 5) will be obtained from all participants prior to

their enrolment in the study. All participants will be scheduled for an initial assessment (approximately 1.5 hours in length) that will begin with a brief interview to complete the demographics questionnaire (ATTACHMENT 11) and the short form International Physical Activity Questionnaire (ATTACHMENT 12)(57). They will then have their height, weight, circumference measurements (biceps, chest, waist, hips, thigh), resting heart rate, and oxygen saturation levels measured (ATTACHMENT 13). Following these measurements participants will complete the lower and upper body physical function assessments (ATTACHMENT 13). Finally participants will be given the option of completing the HRQoL questionnaires (ATTACHMENTS 14 & 15) on site or take them home for completion over the phone.. The questionnaires take approximately 25 to 35 minutes in total to complete. Researchers will document and describe any planned exercise that participants are taking part in. After the eight-week time period all participants will be scheduled for a follow-up assessment that will include all of the baseline measures (ATTACHMENT 17). Participants will also be asked to complete the program evaluation survey (ATTACHMENT 10) that will assist researchers in assessing the feasibility of the study. Both assessment sessions will be supervised by the primary investigator, Elise Cunningham, a Registered Kinesiologist. If the participant indicates any distress, they will be offered the opportunity to skip questions or withdraw and receive no further contact from the research team. If necessary the research team will advise the participant to seek a referral to a mental health professional from their own healthcare providers (e.g. family physician).

6.1.3 Intervention: The intervention group will participate in an eight-week NPW program. It will consist of one supervised group NPW session per week (approximately 1 hour in length) and three independent NPW sessions per week. Participants will be instructed on using the poles either immediately after their initial assessment or on an alternate date that is agreed upon (ATTACHMENT 18). They will be asked to practice for one week using the poles prior to their first group session to account for learning effect. Participants will then be assigned to a specific NPW prescription group (Group 1 - compromised (ATTACHMENT 19), Group 2 - inactive (ATTACHMENT 20) or Group 3 - minimally active and highly active (ATTACHMENT 21)) based on their IPAQ score and the observed ability level during the individual instruction session. Participants will be asked to follow their specific individualized NPW prescription throughout the study. During the group sessions the research team who have been trained in instructing NPW will correct technique, ensure participants are progressing according to the pre-determined exercise prescription and address any questions or concerns. Participants will receive training in exercise to mitigate minor risks and help assure their safety. Also participants will be instructed to closely monitor themselves and to maintain exertion to levels that suit their physical capacity (well below exhaustion). After consent is obtained each participant will be asked to provide the name and contact information of someone that they would like to be contacted should an emergency medical situation occur during their participation in the study. This information will be kept in a secure location separate from the data collection sheets during the assessments and Nordic pole walking sessions. Participants will be told to immediately report any exercise related symptoms to the research team. If there are adverse effects that can't be managed in collaboration with the participant and the on-site researchers, the Emergency Medical System will be initiated and the emergency contact that they have provided will be contacted. Additional supports may be utilized by participants (such as oxygen, tables, walls and chairs). Participants will be provided with the principal investigator's contact information should they have any questions or concerns about completing the Nordic pole walking sessions independently. Participants will be asked, but not compelled to engage in these unsupervised sessions.

To promote program adherence participants will be asked to set exercise related goals

(ATTACHMENT 22) prior to beginning the NPW program. Documentation of program adherence is critical to understanding treatment dose(58). Therefore each time participants complete a NPW session (supervised or at home) they will be asked to make an entry in a journal (ATTACHMENT 23) reporting distance walked, duration, and rate of perceived exertion. On days when participants do not complete a NPW session they will be asked record the reason they were not able to walk. The research team will contact participants over phone on a weekly basis to encourage participation as well as answer any questions or concerns that arise (ATTACHMENT 24). At the end of the program participants will reflect back on the goals they set to see how close they have come to achieving them.

The control group will be instructed to continue their usual daily routine for eight-weeks and will be invited to participate in the same NPW program after this time period.

7.0 Statistical Analysis

Narrative descriptions will be used to address feasibility outcomes. Descriptive statistics (mean, median, standard deviation) will be calculated for any numeric data. Non-parametric tests will be used to compare the intervention and control group due to small sample size; a Wilcoxon signed-rank test to see if changes occurred over time and a Mann-Whitney U test to see if there was difference between groups. A p-value of less than 0.05 will considered significant.

8.0 Data Management and Confidentiality

Participants will be assigned a unique study number for the duration of the study. Only this number will be used on any research-related information collected about the participant during the course of this study, so that their identity as a participant in this study will be kept confidential. Information that contains the participant's identity will remain only with the Principal Investigator and/or designate. The list that matches the participant's name to the unique study number that is used on the research-related information will not be removed or released without the participant's consent unless required by law.

Participant information and the data collected will be kept in separate locked cabinets within Dr. Mika Nonoyama's secure office at UOIT. The locked cabinets will require different keys for access. Furthermore, de-identified data will be stored on the laptop of the Principal Investigator (Elise Cunningham), as well as one of the supervisor's laptop (Dr. Mika Nonoyama) and will backed up on an encrypted USB flash drive. All computerized devices used throughout this study are password protected to reinforce confidentiality.

After the data has been used for this study, it may be utilized again in a secondary use of data, but only in an aggregate way and never in a way in which the participant could be identified.

9.0 Knowledge Translation

Our knowledge translation target audience are health providers and patients who have an interest in and/or actively involved in improving the effects of lung cancer. Our knowledge translation strategy is to provide this audience with a variety of products including: 1) web postings of plain language summary of results on a website designed for this study and with external organization (e.g. The Lung Association); 2) direct dissemination of summary of results (web, social media, brochures); 3) presentations and workshops at relevant clinical conferences (e.g. Canadian Respiratory Conference); and 4) publishing in a peer-reviewed publications.

10.0 Timeline

	Months (May 2015 – July 2016)										
Task	**S**	**O**	**N**	**D**	**J**	**F**	**M**	**A**	**M**	**J**	**J**
Committee Meetings			X			X					
Ethics Applications	X	X									
Prepare Tracking Sheets & Manual	X	X									
Recruit Patients			X	X	X						
Training Research Personnel		X	X								
Data Collection			X	X	X	X	X	X			
Data Analysis							X	X	X		
Write-up								X	X	X	
Presentations								X	X		
Submit Thesis										X	
Defend Thesis											X

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