January 2015

The Role Of Physical Activity In The Quality Of Life Of Cancer Survivors

Apoorva Tewari

The Role of Physical Activity and the CDC Physical Activity Guidelines in the Quality of Life of Cancer Survivors

A Thesis Submitted to the
Yale University School of Medicine
In Partial Fulfillment of the Requirements for the
Degree of Doctor of Medicine

By
Apoorva Tewari
2015

Apoorva Tewari, Nicole Aaronson, Melinda Irwin, Benjamin Judson, Anees Chagpar.
Department of Surgery, Yale University School of Medicine, New Haven, CT.

Beyond its cardiovascular and metabolic benefits, physical activity (PA), may improve the quality of life (QOL) of cancer survivors. However, most studies have been in limited cancer types (breast, colon and prostate) and relatively little focus has been given to its effect on less common cancers. Aim 1 was to conduct a systematic review of the effect of PA on the outcomes of head and neck (H&N) cancer survivors. Aim 2 was to determine the effect of the PA guidelines from the Centers for Disease Control (CDC) on the QOL of a diverse sample of cancer survivors. To do so, we used the results of the 2010 National Health Interview Survey (NHIS). Since the NHIS does not provide verified information regarding cancer severity and treatment, Aim 3 was to determine the effect of meeting the CDC guidelines on QOL after accounting for these variables. This cross-sectional study was conducted at the Breast Center – Smilow Cancer Hospital at Yale-New Haven using patient surveys and treatment information.

In Aim 1 we found that PA improved strength, gait speed, pain, fatigue and physical well-being. In Aim 2 only 10.4% of cancer survivors reported meeting CDC recommendations. Meeting guidelines was associated with good QOL on multivariate analysis. It was also associated with more relationship satisfaction, less fatigue, and better mental and physical health on univariate analyses ($p<0.05$ for all). Lastly, the aerobic guidelines were predictors of good QOL ($p<0.001$), independent of sociodemographic factors, while the strength training guidelines were not ($p=0.948$). In Aim 3, 12% of patients met full CDC PA guidelines, while 60% met aerobic guidelines. On univariate analysis, meeting aerobic guidelines was correlated with higher education level ($p=0.032$), better insurance status ($p=0.014$), and fewer financial problems due to cancer ($p=0.003$). Completion of aerobic activity guidelines was correlated with better QOL ($p=0.051$); meeting strength training and combined CDC guidelines was not, $p=0.618$ for both. On multivariate analysis, aerobic activity remained correlated with QOL ($p=0.030$), independent of sociodemographic and cancer-specific variables. Thus we found that PA, including strength training, improved multiple domains of QOL in H&N cancer survivors. In both diverse national and local clinical samples the CDC aerobic activity guidelines predicted QOL, while those for strength training did not. This association was independent of pathological and treatment related factors. New guidelines may better counsel cancer survivors on strength training for improvement of QOL, and more cancer survivors should be encouraged to meet cardiovascular activity guidelines.

Acknowledgements

I would like to express my deep gratitude to Dr. Anees Chagpar. She has mentored me since the very beginning of medical school when she allowed me to shadow her in the OR. Since then she has taught me how to think effectively with flowcharts and write succinctly with the most thorough edits a girl could ask for. She has inspired me not only with her skills in surgery and research but also with her enthusiasm as a life-long learner and a committed teacher.

I would also like to thank Dr. Benjamin Judson who has been a patient and wise mentor over the past few years. He gave me an early introduction into the specialty that I love and in which I hope to join him in the near future.

Tina Adamzcyk, Meghan Butler, Janine Hoffman and the other members of the Yale Breast Center have been extremely kind and helpful to me, and I know this research would not have been possible without them.

I am also indebted to the Yale Department of Surgery for their strenuous support throughout my medical school experience and for the creation of a learning environment in which a student can find so many wonderful role models in academic surgery.

Finally, I need to thank my parents, who are my source of strength and inspiration. Thank you for constantly pushing me to explore the limits of possibility.

Table of Contents

Background

The experience of cancer is physically and emotionally traumatizing, both due to the disease process itself and due to the treatments that patients must undergo that may include invasive surgeries and debilitating chemoradiation regimens. General issues that affect cancer survivors include pain, fatigue, cachexia, low functional status, and worry about recurrence.[1] Yet, each cancer type is also characterized by its own unique assaults on the quality of life (QOL) of patients. For example, head and neck cancer survivors suffer from dysphagia, trismus, and neck pain while dealing with sometimes severe changes in their speech and appearance.[2] By contrast, breast cancer survivors may deal with weight gain, lymphedema, arm pain, self-image issues, and premature fertility concerns.[3] Due to the improvements in cancer treatments over the past few decades, many patients are living long after their original diagnoses. Thus, their QOL during and after treatment is an increasingly vital concern. In this thesis, I will investigate the effect of physical activity on the QOL of cancer survivors.

Quality of Life in Cancer Survivors

In 1971, a meeting of the Board of Directors of the American Institutes for Research decided on an agenda for the coming decade's research. They determined that an investigation of the QOL of Americans should be a priority. Flanagan published a summary of those efforts in 1978 in which he laid out five domains of QOL with 15 sub-categories in all. The domains were: physical and material well-being, relations with other people, social/community/other civic activities, personal development and fulfillment, and recreation.[4,5] These domains were developed after conducting a qualitative survey of almost 3,000 Americans from diverse backgrounds and geographies

regarding the important events in their lives, their sources of happiness and sadness, and other potential contributors to QOL. These categories were then used to evaluate the QOL of another 3,000 Americans in 1975 based on the fulfillment of the various categories according to their relative importance to each individual. The primary finding of the survey was that most Americans were satisfied with their fulfillment in the categories deemed important to them. However, while over 95% of men and women of all age groups deemed health and personal safety as important or very important, only about 80% of them were satisfied with their status in this category.[5] Thus although QOL research was originally developed in the social sciences, its ultimate adaptation for medical purposes was likely.

In 1975, Dr. W. Bradford Patterson published a groundbreaking article in JAMA arguing for the consideration of QOL in cancer treatment.[6] Noting the then-recently developing ability to prolong life with intensive care despite the loss of many bodily functions, he proposed that assessment of quality oncologic care be based on five metrics. They were, "(1) health, the prospect of cure vs failure; (2) function, the ability to work and the quality of performance; (3) comfort, the freedom from pain and the limitations to activity; (4) emotional response, self-acceptance, anxiety about the future, and social adjustment; and (5) economics, the impact of costs and earning capacity."[6] He argued that cancer therapies could not merely be evaluated based on one metric over any other. Rather, their effects must be assessed holistically based on all domains. This was a novel and needed addition to cancer care, and thousands of subsequent studies have investigated the effects of treatment regimens on QOL.

Quality of Life Instruments

Quality of life is primarily evaluated in 4 research contexts: 1) to identify the QOL issues faced by a population, 2) as one of the outcomes in randomized controlled trials to evaluate efficacy of a therapy, 3) as the outcome for therapies aimed at improving QOL, and 4) as an endpoint to evaluate other health services.[7] There are many factors to consider when deciding which instrument to use for a particular study. The first is the purpose of the study itself: is it examining QOL at one point in time or rather the change in QOL over a span of time? This is to identify whether a discriminative (point in time) or an evaluative (change) instrument is required. Secondly, assessment of the QOL of may be general, pertaining to all diseases or conditions, or specific, pertaining only to one disease process or QOL domain.[8] This feature allows more granularity in results for interventions that are more limited in scope, such as one that decreases the pain after neck dissection. In this scenario, an instrument specifically for head and neck cancer patients may be more appropriate than a generic instrument that describes overall QOL. The mode of administration is also an important factor. Surveys can be optimized for in-person verbal administration, written administration, or phone administration, and their validity may vary if administered differently. Lastly, practical matters such as the amount of time necessary to complete the survey and the language of administration must also be considered.

General QOL instruments are useful for comparing cancer survivors to the healthy population. These instruments, such as the Medical Outcomes Short Form- 36 (SF-36) and the World Health Organization Quality of Life Assessment Instrument (WHOQOL-100) are well-validated options that are available in a variety of languages and have

validated abridged versions.[7] However these instruments do not provide information on the particular symptoms that certain segments of the cancer survivor population may face. The Functional Assessment of Cancer Therapy-General (FACT-G) survey assesses global QOL of cancer patients as well as physical, functional, social and emotional domains. There are also alternative versions of this survey that are tailored to 20 cancer types, 9 treatment modalities, and 16 symptoms. The above instruments also have population-based normative data to which results may be compared.[7]

Physical Activity: Definitions and Measurement

Every year, Americans spend $124 billion in the treatment for cancer patients.[9] As we seek to address the QOL issues of cancer survivors, an option that would cause the least economic burden would be optimal. Physical activity is one such factor that is an inexpensive and powerful adjunct to medical care. In 1985, Caspersen et al defined physical activity as "any bodily movement produced by skeletal muscles that results in energy expenditure."[10,11] Since then this definition has been modified by Winter and Fowler who include isometric muscle exercises in the definition of physical activity, despite the fact that it does not involve bodily movement.[12] Physical activity was subsequently subdivided into categories of occupational and leisure. Exercise is a sub-category of leisure time physical activity that is "structured and repetitive physical activity designed to maintain or improve physical fitness."[13]

The National Institutes of Health recommends that Americans engage in four types of physical activity: aerobic, strength, balance and flexibility training.[14] Aerobic activity involves activity that requires increased breathing and heart rate. Strength training involves movement or isometric motion against resistance. Resistance can be defined as

body weight, resistance bands or weights. Balance training involves forcing one's body to sustain itself in space in controlled settings such that proprioception and core muscle strength are improved. Finally, flexibility training stretches muscles and ligaments to improve range of motion and decrease injury. Some types of exercise may fall into multiple categories, such as Pilates that provides strength, balance and flexibility training.

Of the types of physical activity, primarily aerobic activity is broken down based on the intensity of exercise. These methods are commonly utilized both for research and for practical purposes. Intensity can be evaluated as either absolute or relative intensity. Absolute intensity is a rating of the energy used by the body during each minute of the activity. One method is use of the heart rate during activity as a proportion of maximal heart rate. Moderate activity is 50-70% of a participant's maximal heart rate, while vigorous activity is 70-85%. A person's maximal heart rate varies primarily with age, so the optimal range must be calculated for each participant.[15] Another method, which will be used in this thesis, is metabolic equivalent units (METs), which are categorized such that 1 MET is equivalent to the energy expended by a person at rest, often standardized to 1 kcal/kg/hr, though the real value varies for each person based on age, sex and body surface area.[15] Sedentary activity (e.g. standing) expends < 1.5 METs, light intensity activity (casual walking) expends 1.5-2.9 METs, moderate activity (brisk walking) expends 3-5.9 METs, and vigorous activity (jogging/running) expends ≥ 6.0 METs.[16] By contrast, relative intensity is a tool for participants to gauge their current effort. An example of this is the talk test, in which a participant can talk, but not sing, during moderate activity, while she can only say a few words without stopping for breath during vigorous activity.[17] There are also metrics for the measurement of strength training

intensity that are based on fraction of maximum contraction force of a muscle group. However, they have not been studied enough for the development of guidelines or recommendations.

Physical Activity and Cancer Survivors

The Centers for Disease Control (CDC) and the American Cancer Society (ACS) recommend that everyone, including cancer survivors, participate in at least 150 minutes of moderate or 75 minutes of vigorous physical activity, along with 30 minutes of strength training every week.[18] Aside from certain populations with contraindications to exercise (Table 0.1), physical activity is considered generally beneficial.[19,20] The benefits of physical activity for cardiorespiratory fitness, muscular strength, endurance and flexibility have been well established in the general population.[13] These advantages also apply to cancer survivors who often suffer from deconditioning due to their disease and its treatment.[21] Exercise, both pre- and post-diagnosis, is also associated with improved survival in breast cancer, colorectal cancer and prostate cancer.[22] The mechanisms of these protective effects are thought to be related to the role of physical activity in anti-inflammatory processes, immune regulatory function and hormonal regulation.[23] Physical activity is also important in the prevention of diabetes and the control of blood sugar, which have been implicated in the pathogenesis of breast and prostate cancers.[24,25] A potential model of the effects of physical activity is displayed in Figure 0.1 from the book Physical Activity, Dietary Calorie Restriction, and Cancer.[26]

A Cochrane review of the effect of physical activity on the QOL of cancer survivors found that it is associated with improved global health related QOL.[27,28] Of the domains

of health related QOL, physical activity was associated with improved body image, emotional well-being, sleep regulation, psychological health, fatigue, pain, sexual health and social functioning.[27] A small number of studies suggested an association between exercise and depression and body image. No conclusions could be drawn for the relationship between physical activity and "cognitive function, physical function, general health perspective, role function, and spirituality," though some studies suggested an association.[27,29] However, most of these studies were conducted in breast cancer patients who do not necessarily deal with the same insults to their QOL as do patients of other cancers such as head and neck or lung. Head and neck cancer patients, for example, have issues with cachexia rather than obesity, and the hormonal factors implicated in breast and prostate cancers are not relevant in this cancer type. Thus it is possible that the effect of physical activity in such a population may be different from its effect on patients with more common cancer diagnoses. Furthermore, although physical activity has been shown to improve quality of life, the efficacy of the current guidelines in achieving this goal has not been evaluated. Thus, the goals of this thesis are to examine the effect of physical activity in a less-studied cancer type and to determine the efficacy of the CDC physical activity guidelines in improving the quality of life of cancer survivors.

Specific Aims

The purpose of this thesis is to investigate the role of physical activity and the CDC physical activity guidelines in the quality of life all cancer survivors, including those with less commonly studied diagnoses. Aim 1 is to understand the ways in which physical activity affects the quality of life cancer survivors. Since most of the studies regarding quality of life and physical activity in cancer survivors were conducted in breast cancer patients, the Cochrane reviews cited above were stilted towards this cancer type. For that reason, studies of survivors of a less-common cancer type, Head and Neck cancer, were systematically reviewed. Although obesity and hormonal influences are thought to be less relevant in this cancer type, we hypothesize that there will be a positive influence of physical activity on the quality of life of these patients.

Aim 2 will evaluate whether the CDC guidelines for physical activity result in an improvement of the quality of life of a diverse population of cancer survivors. It will also provide important ecologic information regarding the compliance with CDC physical activity guidelines among cancer survivors. Aim 3 was developed in response to the perceived weaknesses of the methods in Aim 2 in which objective pathologic and treatment data were not available. In Aim 3, we verify in a local sample of breast cancer survivors whether meeting CDC guidelines was correlated with improved quality of life independent of cancer and treatment related factors. We hypothesize that while CDC guidelines will be correlated with improved quality of life, the majority of cancer survivors will be found not to meet the guidelines.

Methods

Aim 1: Systematic Review

Study Retrieval and Selection:

A systematic search in PubMed, Embase, and Web of Science was conducted for the effect of physical activity on head and neck cancer patients. (Table 1) Relevant synonyms for the search terms physical activity, QOL, and survival were included. Two authors (A.T. and N.A.) excluded duplicate titles and independently screened the resulting titles and abstracts for inclusion. Only reports of original study data were included; systematic reviews, opinion papers, animal studies, and case reports were excluded, as were non-English studies. Studies of rehabilitative exercises and physical therapy for dysphagia were also excluded. Additionally, PubMed, Web of Science and Embase were searched for related articles and references not identified in the initial literature search.

Assessment of Sources:

The remaining articles were assessed for relevance and risk of bias using predefined criteria by two of the authors (A.T. and N.A.) (Table 2). Relevance concerned the applicability of the study findings to the clinical question and involved the evaluation of patients and compared treatments and outcomes. Risk of bias was evaluated based on randomized treatment allocations, standardized treatment, standardized outcome and completeness of data.

Data Extraction:

Two authors (A.T. and N.A.) independently extracted descriptive data of patients and treatments for the remaining references. Outcome data were pooled according to categories of outcomes (survival and domains of QOL) regarding the relationship between physical activity and head and neck cancer.

Aim 2: NHIS

Data regarding QOL, physical activity and other covariates were obtained from the 2010 National Health Interview Survey (NHIS), the largest source of health information for the United States non-institutionalized, civilian population.

NHIS Survey

The NHIS is a cross-sectional, population-based, face-to-face interview survey conducted annually by the National Center for Health Statistics (NCHS). Every year the survey is administered by the Census Bureau in 428 regions chosen from 1900 that cover the 50 states and the District of Columbia. The weighted sample is designed to reflect the civilian non-institutionalized population of the United States. The final weights are also adjusted according to age, sex, race, and ethnicity classes based on population estimates produced by the U.S. Bureau of the Census. The sample is re-evaluated every 10 years, using the most recent Census information. The sample is chosen in such a way that each person in the population has a known non-zero probability of selection. The current design includes oversampling of Black, Hispanic and Asian persons to obtain statistics that can be generalized to these populations. For example, any black, Asian, or Hispanic adult aged 65+ years has twice the chance of being selected as the sample adult as any other adult. The 2010 NHIS included a cancer supplement, which provided information

as to personal history of cancer, recurrence and perceived risk of recurrence. The final response rate for this portion of the survey was 60.8%.

Cancer Survivors

Cancer survivors were defined as those who reported having had been told that they had cancer, excluding non-melanomatous skin cancers.

Physical activity

Survey participants were asked several questions regarding their physical activity. These questions were developed to determine the amount of vigorous and light/moderate physical activity the participants engaged in, as well as their participation in strength training exercise. Each participant was asked how often he/she engaged in at least 10 minutes of vigorous exercise and how long they exercised each time. Similar questions were asked regarding their light/moderate exercise as well as their strength training habits. In our analysis, meeting guidelines for physical activity was divided into the CDC guidelines for cardiovascular and strength training. The cardiovascular guidelines entailed engaging in 150 minutes of moderate-intensity exercise per week, 75 minutes of vigorous-intensity exercise per week, or some combination thereof. In order to tabulate the total amount of cardiovascular activity each participant completed, taking into account intensity, a short-hand calculation was used. In this calculation, the number of minutes of cardiovascular exercise was converted into metabolic equivalents (METs) per week of exercise, where one hour of vigorous exercise was 8 MET-hr/week and one hour of moderate exercise was 4 MET-hr/week. The total number of MET-hrs/week were added together, and completion of 10 MET-hr/week was equivalent to satisfying the

cardiovascular activity guidelines. Strength training guidelines involved 2 sessions per week.

Quality of Life

Quality of life was determined by the answer to the question, "In general, would you say your QOL is "*excellent*", "*very good*", "*good*", "*fair*" or "*poor*". Other questions related to QOL related to ratings of fatigue, physical health, mental health, and relationships had the same response structure. For the multivariate analysis, the responses were dichotomized into good QOL (including responses of excellent, very good and good), versus not good QOL (including responses of fair and poor).

Due to its extensive follow up probes that provide deep insight into each domain, the quality of life assessment in the NHIS is considered more thorough than self-administered instruments such as the standard form-12 (SF-12) or the EuroQol EQ5D.[30] In comparison to the Behavioral Risk Factor Surveillance System (BRFSS) and the Current Population Survey (CPS) over a 10-year period, the NHIS was found to have similar rates of respondents reporting excellent health.[31] Both the NHIS and the CPS also had similar trajectories regarding proportion of respondents reporting fair/poor health, while the BRFSS found a more negative trajectory with more respondents reporting fair/poor health. However, this discrepancy was thought to be due to the home phone-interview methodology of the BRFSS, which selected for older respondents who were generally less healthy.[31]

Statistical analysis

Statistical analysis was performed using SAS Version 9.1.3 and SUDAAN software. Univariate analysis of meeting CDC guidelines and self-reported quality of life was conducted using chi-square analysis. The Taylor series was chosen as the method of variance estimation. Multivariate analyses were conducted using logistic regression. The Taylor series was used for variance estimation and robust standard error method calculation was used.[32]

Aim 3: Cross-sectional study

Institutional Review Board approval was obtained for a cross-sectional study of patients diagnosed with breast cancer who were seen at the Breast Center-Smilow Cancer Hospital at Yale-New Haven between September-December 2013 who were recruited to answer a short survey regarding physical activity and QOL. Questions were modeled so as to be analogous to those asked in the NHIS. Of the 79 surveys returned, 50 were completed (QOL and physical activity responses) such that analysis could be done. The survey is attached in the appendix. Analysis was done on Wizard 1.6 software.

Statement of Student Contribution

I, Apoorva Tewari, was involved in hypothesis generation, study design, data collection and analysis of the aims of this thesis. I was also involved in all writing and editing that occurred for the 2 papers that were submitted to journals for this research. In specific:

Aim 1: With the help of Dr. Judson I generated the hypothesis and research design for the systematic review of the effect of physical activity on head and neck cancer patients. I conducted a literature search and extraction that was duplicated by Dr. Aaronson, in accordance with research practices for systematic reviews. I then compiled the results and discussion sections with input from Dr. Judson and Dr. Aaronson.

Aim 2: With the help of Dr. Chagpar, I generated the hypothesis and research design for the cross-sectional study using the National Health Interview Survey. I conducted the statistical analysis with SUDAAN software and interpreted the results. Dr. Chagpar provided very important insights at the time of analysis, during the interpretation of the results and in writing up the final manuscript. Dr. Irwin provided valuable context for the research.

Aim 3: With the help of Dr. Chagpar, I generated the hypothesis and research design for the cross-sectional survey at the Breast Center- Smilow Cancer Hospital at Yale-New Haven Hospital. With Dr. Irwin's recommendation we chose a physical activity survey, and I along with Karen Stavris and Tina Adamczyk implemented the survey. I input the data and ran statistical analysis. With Dr. Chagpar's input, I interpreted the data and wrote up the results.

Results:

Aim 1: Systematic review

A total of 361 titles were retrieved, of which 274 were unique (Figure 1, date of last search was December 14th, 2014). Six additional titles were identified from screening the references of the selected articles. After screening titles, abstracts and full-text articles, 256 references were excluded, after which 16 articles remained.

Of the 16 references that met the inclusion criteria, 6 were randomized controlled trials, 3 were cross-sectional studies, 5 were cohort studies, and two were non-randomized controlled clinical trials (Table 2). None of the studies were blinded. The total number of patients in all samples was 1,583. The types of physical activity assessed in the studies varied from standardized walking regimens and self-assessed physical activity levels to resistance training programs. One commonly investigated intervention was resistance training, which was often chosen instead of aerobic training for the duration of radiation therapy due to the comorbidities of head and neck cancer patients. Progressive resistance training was defined as incrementally increased resistance as muscular strength increased.[33,34] Among the cross-sectional studies, methods of assessing physical activity included Godin and PASE surveys. An overview of the QOL surveys used in the studies is given in Table 2. The outcomes evaluated in the studies varied and included QOL, functioning, strength, sleep disturbances, pain and fatigue (Tables 4-7).

Data Analysis:

One study examined the effect of physical activity on the survival of head and neck cancer patients.[35] Duffy et al evaluated the effect of pre-diagnosis health behaviors including exercise, smoking, alcohol consumption, sleep and diet on 5-year survival after

head and neck cancer diagnosis. While physical activity was correlated with survival on univariate analysis with a $p<0.001$, this relationship did not persist on multivariate analysis with $p=0.085$ after accounting for smoking, age, education, tumor site and stage.[35]

Seven studies examined the effect of physical activity on overall QOL. The Rogers et al studies from 2006 and 2013 assessed QOL via FACT-G and FACT-H&N surveys.[36,37] In the cross sectional study from 2006, the relationship between exercise and overall QOL as measured by FACT-G was insignificant ($p>0.05$).[36] In the RCT from 2013, the progressive resistance-training group had a blunting of the deterioration of QOL that occurred in the control group during radiotherapy. In the 27-question survey scored from 0-112 points, the difference in QOL between the control and intervention groups was 7.4 points at 6 weeks and 6.6 points at 12 weeks, where a 4.4-point difference is clinically relevant for the overall score. The McNeely et al studies, both RCTs from 2004 and 2008 also examined the effect of progressive resistance training on QOL via FACT-G.[33,34] The first, from 2004, compared progressive resistance training with independent exercise, and found no difference in overall QOL ($p=0.82$).[33] The second, from 2008, compared progressive resistance training with standard physical therapy and also found no difference ($p=0.09$).[34] With regards to head and neck specific QOL, neither the Rogers et al randomized controlled trial [37] nor the McNeely 2004 study found a significant difference between the training and control groups.[33] However, the Rogers et al cross-sectional study found that the relationship between amount of physical activity and disease-specific QOL as measured by FACT-H&N approached significance with $p = 0.064$.[36,37] Eades et al and Lonbro et al used the Modified Edmonton Symptom

Assessment System and the EORTC QLQ-C30 questionnaires, respectively.[38,39] Eades et al found a moderate effect of exercise on overall QOL, with an effect size of 0.8.[38] Effect size was calculated by dividing the mean changes by the standard deviations of the mean changes. Lonbro et al found that early exercise, within the first twelve weeks of diagnosis, resulted improved overall QOL relative to delayed exercise, in the subsequent 12 weeks. ($p<0.05$). [38,39] The abstract by Zhou et al found less of a decline in QOL (measured with SF-36) in the exercise group compared to control. However, no p value was given for these data.[40]

Four studies examined the relationship between physical activity and physical well-being. The Rogers et al RCT found that a resistance-training program resulted in a clinically relevant improvement in physical well-being of patients undergoing.[37] In a RCT by Samuel et al, physical well-being in the training group stayed the same 6 weeks after commencement of radiation therapy, while the physical well-being of the non-exercise control group was lower with p value approaching significance (0.064).[41] By contrast, neither the Capozzi et al ($p=0.16$) nor the McNeely et al ($p=0.67$) studies found an association between exercise and physical well-being after the full length of the exercise program.[33,42] However, the Capozzi et al study did find that in the acute setting, the training sessions resulted in improved feelings of well-being at the end of the session when compared to the beginning of the session ($p=0.01$).[42]

Weakness and decreased physical functioning are also important concerns for head and neck cancer patients. Five studies demonstrated that exercise after beginning radiation therapy treatment resulted in significant improvements in strength.[34,38,39,43,44] While three studies found no association between exercise training and improved

strength,[33,37,42] the six studies that investigated the association between physical activity, resistance training and Tai Chi all found that these were associated with increased gait speed in participants.[38,39,42,43,45,46] The McNeely study from 2004 found no association between physical activity and shoulder disability, and a later study by McNeely published in 2008 found that shoulder disability was improved in those engaging in progressive resistance training as opposed to standard physical therapy.[33,34,38]

Two studies investigated the role of exercise on physical function. Lonbro et al, in their study examining the difference between early (between 0-12 weeks) and delayed (between 12-24 weeks) exercise after radiation therapy for head and neck cancer, showed that both early and delayed exercise improved physical function significantly ($p<0.05$) relative to the beginning of the study.[39] However, Rogers et al found no association between resistance training and physical function at 6 weeks or 12 weeks ($p>0.10$) in their randomized controlled trial.[37] Eight studies investigated the role of physical activity in the fatigue experienced by head and neck cancer patients. Five studies suggested an association between exercise and decreased fatigue[47,48,37,39,42,48,49] two showed no effect ($p>0.05$)[34,50] and one showed a marginal effect.[36]

Many head and neck cancer patients experience various somatic symptoms as a result of their disease and its treatment. These include pain, shortness of breath, anorexia, insomnia, nausea, vomiting constipation, and sleepiness. Five studies examined the relationship between pain and physical activity.[33,34,38,42,51] Four of the studies found that strength training and other physical activity were associated with decreased pain, while Capozzi et al found no effect either over the whole program or after each session. Both Eades et al and Capozzi et al investigated shortness of breath.[38,42] While the Eades et al

study found a moderate effect of physical activity on shortness of breath, Capozzi et al found no association, either in the acute setting or after completion of the whole program. With regards to appetite, too, the Eades et al study found a moderate association, while Capozzi et al found none.[38,42] Both Capozzi et al and Eades et al had negative results for nausea and sleepiness' associations with physical activity.[38,42] Three studies investigated physical activity and insomnia. While Eades et al found a moderate association with effect size=0.6, the 2008 Rogers et al found no association ($p>0.05$). Although Zhou et al found trends indicating decreased sleep disturbance in the exercise group, though their sample size was not sufficient for full conclusions to be made. Eades et al also did not find an association between physical activity and constipation.[38]

Several studies have also evaluated mood, worry and overall emotional well-being. With regards to emotional functioning and well-being, Rogers et al found clinically relevant group differences.[37] By contrast, the Lonbro et al study found that one of their exercise groups had improved emotional functioning relative to baseline, while the other did not.[39] Similarly, McNeely et al also found that emotional well-being was not significantly improved in the progressive resistance exercise group compared to control ($p=0.89$).[33] The Eades study found that although exercise had a moderate effect on depression, it had a small effect on mood.[38] However, two other studies found no association between the full exercise program and decreased depression, though Capozzi et al did find that depression improved from the beginning to the end of each session.[36,42] Two studies examined the role of physical activity in worry.[38,42] Eades found a small association between physical activity and worry and a moderate effect of physical activity on distress. Capozzi et al found that the feeling of anxiety was improved after each

resistance exercise session (p=0.01), while its improvement at the end of the full 12-week exercise program approached significance (p=0.06).

Samuel et al found that cognitive function was also improved in the group randomized to a 6 week walking and resistance training program ($p<0.05$) while the control group experienced decreased cognitive function ($p<0.05$) during the same period.[41] Another study found similarly that those participating in early exercise after radiation therapy experienced significant improvement in cognitive function in the first 12 weeks while those who had not begun the exercise intervention experienced a decline in cognitive function ($p<0.05$).[39] The 2008 Rogers et al cross-sectional study, however, failed to show a significant relationship between exercise and cognitive function in head and neck cancer patients ($p>0.05$).[50]

Three studies examined the effect of exercise on social well-being. One randomized controlled trial found that early exercise after radiotherapy resulted in improved social function relative to baseline at 24 weeks ($p<0.05$), but not at 12 weeks or relative to delayed exercise ($p>0.05$). Delayed exercise did not result in improved emotional function at either time point ($p>0.05$).[39] The other two studies also found no significant relationship between physical activity and social functioning.[33,37] Eades et al found small effect sizes in the role of exercise on ability to work, enjoyment of life, and function with general activity.[38] Another trial found that early exercise after radiotherapy resulted in improved social function relative to baseline at 24 weeks ($p<0.05$), but not at 12 weeks or relative to delayed exercise ($p>0.05$). Delayed exercise did not result in improved social function at either time point ($p>0.05$).[39] Three studies investigated the effect of exercise on functional well-being. The first, a cross-sectional study, found a small effect (Pearson

correlation coefficient= 0.3, p=0.027), and a randomized controlled trial found that resistance training resulted in clinically relevant improvements in the functional well-being of patients undergoing radiotherapy.[36,37] Another RCT found no association with functional well-being.[33]

Aim 2: NHIS: Quality of Life

In 2010, 2333 cancer survivors were surveyed, representing 19,441,052 people in the US population. Of these, only 10.4% met the full CDC physical activity guidelines with 23.0% meeting just cardiovascular guidelines and 19.9% meeting just strength training guidelines. The univariate and multivariate analysis of sociodemographic factors and cancer type with meeting guidelines is shown in Table 2.1. On univariate analysis, age ($p<0.001$), race ($p=0.002$), education ($p<0.001$), insurance status ($p<0.001$), marital status ($p<0.001$), employment status ($p<0.001$) and type of cancer ($p<0.001$) were correlated with completion of CDC guidelines. However, on multivariate analysis, only higher level of education was significantly correlated with increased likelihood of satisfying guidelines ($p<0.001$). Those with a professional degree were 14 times more likely to follow guidelines than those with less than a high school education (OR=14.25, 95% CI: 3.58-56.70).

Nearly a quarter of all cancer survivors (23.0%) claimed that they met the cardiovascular activity guideline of 10 METs per week. Factors associated with meeting these cardiovascular guidelines are shown in Table 2.2. On univariate analysis, all factors, including sex, age, race, education, insurance status, marital status, employment status and type of cancer were correlated with adherence to CDC cardiovascular activity

guidelines with p<0.001. On multivariate analysis, age (p<0.001), race (p=0.016), education (p<0.001) and type of cancer (p<0.001) were all independent predictors of meeting cardiovascular guidelines. Gender approached significance (p=0.056) with female cancer survivors being roughly half as likely to meet aerobic activity guidelines as men (OR= 0.59, 95% CI: 0.34-1.01).

In terms of strength training, 19.9% of cancer survivors surveyed completed two sessions of strength training per week. While on univariate analysis, sex (p=0.025), age (p=0.002), race (p=0.002), education (p<0.001), insurance status (p=0.012), marital status (p=0.001) and employment status (p=0.008) were associated with completion of CDC strength training guidelines, only education (p<0.001) remained an independent predictor on multivariate analysis (Table 2.3).

Adherence to cardiovascular, strength training and overall guidelines were all associated with more favorable ratings in all aspects of QOL (all p<0.001, Table 2.4).

Factors correlating with "good or better" QOL on multivariate analysis are shown in table 5. Meeting all guidelines was significantly correlated with good QOL independent of other factors (OR: 4.42, 95% CI: 1.26-15.49, p=0.021). In order to understand the relative contributions of aerobic and strength training on QOL, a second multivariate model including these two guideline metrics, was run (Table 2.6). Only aerobic activity was independently associated with good QOL (OR: 3.30, 95% CI: 1.48-7.35, p=0.004).

Aim 3: Cross-sectional study

Of the 79 patients recruited to the study, 50 had provided responses for both the physical activity and quality of life sections of the survey. In Table 3.1, an outline of the sociodemographic and cancer-specific characteristics of the sample is given. Twelve percent of respondents met CDC physical activity guidelines for both aerobic and strength training, while 48% met the aerobic guidelines alone. All those who met strength-training guidelines had also met aerobic guidelines. The univariate analysis of sociodemographic and cancer-treatment factors associated with meeting CDC physical activity guidelines is shown in Table 3.2. No sociodemographic factor was significantly correlated with completion of CDC guidelines, though education approached significance with $p=0.059$. The univariate analysis of factors associated with meeting aerobic guidelines is shown in Table 3.3. Education level, insurance status, and financial difficulties due to cancer were significantly correlated to completion of aerobic guidelines with $p=0.032$, $p=0.014$ and $p=0.003$, respectively. The proportion of patients who either met or did not meet aerobic activity guidelines based on education, insurance coverage and financial difficulty categories is shown in Figure 3.1.

The majority of patients (92%) reported their QOL to good, very good or excellent, while only 8% reported a poor or fair QOL. The distribution of QOL in this sample is shown in Figure 3.2. The univariate analysis of factors associated with overall QOL is shown in Table 3.4. In this analysis, higher education level ($p=0.019$), private insurance coverage ($p<0.001$), fewer financial concerns due to cancer ($p=0.013$), lack of lymph node surgery ($p<0.001$), positive estrogen ($p=0.001$) and progesterone receptor status ($p=0.029$), lack of lymphovascular invasion ($p=0.020$) and completion of aerobic activity guidelines ($p=0.051$) were correlated with better overall QOL. Meeting strength

training and overall CDC guidelines was not correlated with overall QOL, with p=0.618. On multivariate analysis, aerobic activity remained significantly correlated with overall QOL (p=0.030), independent of education, financial concerns due to cancer, and nodal surgery. Meeting aerobic guidelines was also correlated with physical QOL (p=0.045) and social QOL (p=0.003), though it was not correlated with mental QOL (p=0.104). Meeting the strength training and overall physical activity guidelines were not correlated with any domain of QOL (physical health, mental health or social activities and relationships) ($p>0.05$ for all).

Discussion:

Aim 1:

Interest in physical activity as an intervention in cancer patients is growing. Physical activity has been shown to improve survival in colorectal, prostate, and breast cancer survivors and has been shown to improve QOL in cancer patients at large.[28,52-56] In this thesis, I sought to investigate the effect of physical activity on the QOL of cancer survivors. To do so, I first examined the current data regarding the role of physical activity in the outcomes of head and neck cancer survivors, where there is limited consensus. A systematic review of recent literature was conducted to investigate the role of physical activity in the survival and QOL of this population.

The reported effect of physical activity on overall QOL appears to vary based on survey instrument used. General cancer QOL instruments such as the modified Edmonton Symptom Assessment System and the EORTC QLQ-C30 were more sensitive to improvements in QOL brought about by physical activity in head and neck cancer survivors.[38-40] However, surveys that were more specific to the QOL concerns of cancer survivors or head and neck cancer patients were less likely to be affected physical activity.[33,34,36,37] Mechanistically, this distinction makes sense as physical activity is unlikely to affect head and neck specific symptoms such as dysphagia and dysphonia. The studies using FACT-G had mixed results, possibly because it has characteristics of both a general (lack of energy) and cancer-specific QOL instrument (side effects of treatment).[33,36,37]

In this systematic review, physical activity seems to be associated with improved physical function. Physical function is the extent of someone's ability to carry out their normal activities without being limited by their physical capabilities. There is a diversity

of methods to evaluate physical function. The two general categories of assessment are questionnaires and exercise tests. Surveys such as the EORTC QLQ-C30 and the SF-36 have sections devoted to the assessment of physical function by asking about a subject's ability to walk, climb stairs and conduct the activities of daily living. The advantage of these is their ability to give holistic information about a subject's ability to live independently. Furthermore, certain surveys such as the Brief Fatigue Inventory (BFI), provide insight into physical limitations due to particular symptoms. However, exercise tests such as the six minute walk test or hand grip strength provide an objective assessment that can also be a valuable asset in assessment. In this systematic review, a wide variety of assessment methods were utilized allowing multiple perspectives on the effect of physical activity on the physical function of head and neck cancer survivors.

Of the eight studies investigating the effect of physical activity on muscle strength, five found an improvement in strength in those who exercised.[33,34,37-39,42-44] The randomized clinical trial by Rogers, however, did not find a similar effect. This may have been influenced by their chosen methodology to evaluate strength.[37] They found that patients who had undergone neck dissection and were experiencing neck, shoulder or back pain were not able to exert their full effort using the back-leg dynamometer, thus systematically underestimating muscle strength and possibly contributing to the lack of improvement seen in the intervention group. Had strength been measured by bicep curl or other movement, the measurement would not have been limited by pain due to the neck dissection. Capozzi et al's study from 2014 also did not find that grip strength improved after the physical activity intervention.[42] However, this was the only measure used to

evaluate strength in this study, in contrast to the knee extension/flexion and arm curls used in others, which did show an improvement after the exercise interventions.

Gait speed was uniformly improved by several types of physical activity ranging from independent exercise to progressive resistance training to Tai Chi.[38,39,42,43,45,46] Four out of the five studies investigating the relationship between pain and physical activity in head and neck cancer patients found that pain decreased with increased physical activity.[33,34,38,42,51] The only exception was the Capozzi et al trial.[42] However, this study suffered from a potential selection bias as 47.6% of its participants dropped out of the 12-week progressive strength training program in order to go back to work since the strength training sessions were held on weekday afternoons. Thus it is possible that those who remained were the ones who were in the most pain or dealing with other symptoms that prevented them from going back to work; analysis of the symptoms affecting those who dropped out and returned to work was not conducted.

Fatigue is a common symptom faced by head and neck cancer patients; one cross-sectional survey reported that 33% of head and neck cancer survivors deal with fatigue one year after completing treatment.[57] Radiation is well-recognized as a cause of fatigue, particularly during treatment.[58] In this systematic review, we found that the relationship between fatigue and physical activity was related to receipt of radiation therapy. Those studies limited to patients currently undergoing radiation therapy found an improvement due to physical activity, while populations that were not predisposed to fatigue by radiation did not have a significant imkprovement.[34,36,37,39,42,48-50] Thus, the increased fatigue caused by radiation therapy may be improved by physical activity.[59] A range of other symptoms has also been studied. While two studies found an improvement in

insomnia with physical activity, a cross-sectional study found no association.[36,38,40] However, no large RCTs have been conducted to investigate this topic. No association could be determined between physical activity and sleepiness, shortness of breath, anorexia, nausea, vomiting and constipation.[38,42]

The effect of physical activity on overall physical function was evaluated by two studies. Both studies had similar interventions of 12 weeks of strength training exercises, but they used different methodologies of evaluating physical function and had different findings. While the Lonbro et al study found improved physical function in the intervention group, the Rogers et al RCT did not.[37,39] The studies used slightly different samples of patients, in which Lonbro et al used patients who had completed their radiation therapy, while the Rogers et al RCT intervened on patients currently undergoing radiation therapy. Thus it is possible that improvement in physical function due to physical activity was not sufficient to improve QOL of patients undergoing radiation therapy. However, this is at odds with the data regarding fatigue, in which fatigue appeared to be preferentially improved in those undergoing radiation therapy. Another possible account for the lack of effect seen in the Rogers et al study is that the first 6 weeks of exercise were supervised at the radiation facility while the latter 6 weeks were independently done at home. During the second six weeks, adherence dropped to 53%. Lack of adherence to the exercise regimen while at home may skew the data toward the null hypothesis, while the patients in the Lonbro et al intervention were supervised throughout. However, a midpoint evaluation of QOL was not conducted to confirm this theory. Furthermore, as a pilot study, the Rogers et al RCT was powered to study the feasibility of a physical exercise regimen on head and neck cancer patients, not its

efficacy. In their discussion, they mention that a future study would require a sample size of more than 100 participants to see an effect in physical functioning. Lastly, the methods of evaluating physical function were quite disparate. While the Lonbro study used a survey, the EORTC QLQ-C30, the Rogers RCT used a battery of physical function tests such as chair rise-and-sits and balance. Physical activity may improve the holistic physical status of head and neck survivors in ways that cannot be evaluated by standardized exercises that break down physical function into particular parameters. However, with each study using disparate methods, and one being a pilot study, these results are preliminary. Similar to overall physical function, the data regarding overall physical well-being were also inconclusive. While two randomized controlled trials found exercise improved physical well-being, two other studies, one a single arm interventional cohort and the other an RCT, found no effect. However, all of the studies had small sample sizes and used disparate instruments in evaluating physical well-being, making comparison difficult.

Despite the importance of emotional well-being, social well-being, functional well-being and cognitive function to patient QOL, such factors are difficult to assess in a standardized fashion. Multiple factors affect a patient's sense of emotional well-being making it difficult to show a strict causal relationship of physical activity. While there is some evidence that depression and emotional well-being may be improved by physical activity, there is limited evidence for an effect on mood, relations with others and social functioning.[33,37-39,42] The beneficial effects of physical activity may also depend on the context of the exercise, the participant's socioeconomic background, whether the activity encourages interactions through a group class and whether a participant responds well to

competition.[60] The correlation coefficient of physical activity on ability to work, enjoyment of life, and general activity are all below 0.4, suggesting a small to negligible effect.[38] However, physical activity did appear to benefit cognitive function and functional well-being in two out of the three studies.[33,37,39,46,50] Larger RCTs are required to better understand these relationships as the sample sizes were small and the study designs were varied.

Aim 2:

Given the promising effects of physical activity in some domains of QOL in head and neck cancer, the impact of meeting CDC physical activity guidelines on the QOL of all cancer survivors in the United States was next examined. Only 10.4% of Americans diagnosed with cancer report satisfying the CDC guidelines for physical activity with 23.0% satisfying the cardiovascular guidelines and 19.9% satisfying the strength training guidelines. No other study has evaluated compliance with both the cardiovascular and strength training requirements. Most have been concerned with the cardiovascular guidelines, despite the fact that the current guidelines have been in place in 2008.[61] Results from NHANES data from 2003-2006 suggest that only 13% of cancer survivors met cardiovascular activity level guidelines.[62] By contrast, in this study, 23% of cancer survivors met cardiovascular guidelines. The data from the NHANES study were obtained via accelerometer, which provided an advantage of objectivity over self-report. However, by excluding feedback from the 53% of total respondents who did not provide sufficient accelerometric feedback, this study was subject to selection bias. Furthermore, its sample size was 126 after selecting for only patients diagnosed with breast, colon,

prostate or endometrial cancer. Our study, by contrast, provides data for 14 unique cancer types. Thus, though our study has the advantage of providing data about a wide variety of cancer types, it lacks objective activity measurement. In 2014, the CDC published a survey of physical activity in American cancer survivors using the 2009 Behavior Risk Factor Surveillance System (BRFS) survey. This study found that 47% of survivors met cardiovascular activity guidelines; again, adherence to strength training guidelines was not evaluated.[63] This statistic is twice the 23% compliance with cardiovascular guidelines found in our study. However, the BRFS study limited the age of cancer survivors to 45-65 years, only included the six most common cancer types, and excluded those within a year of their treatment. By contrast, 44% of our study participants were over the age of 65, a category that was associated with decreased likelihood of meeting cardiovascular guidelines. Furthermore, by only including breast, bladder, cervical, colon, prostate cancer and melanoma survivors, the BRFS study excluded lung and kidney cancer survivors who, according to our results, had some of the lowest cardiovascular activity rates (5.7 and 9.1%, respectively) and included melanoma and cervical cancer survivors who have the highest activity rates (40.8 and 40.3%). Thus, the high compliance rates found by the BRFS may be due to selection bias.

In our study, meeting CDC physical activity guidelines was predictive of increased odds of having good QOL. On univariate analysis this association held with multiple domains of QOL including fatigue, physical, mental and social/relationships. These results reinforce findings from Phillips and McAuley who demonstrated that physical activity was significantly correlated with improved global QOL along with physical, emotional, functional and social well-being in a longitudinal sample of breast cancer survivors.[64]

They demonstrated that this improvement was mediated by the increased self-efficacy cultivated by exercise.[64] Santa Mina et al also found that meeting cardiovascular activity guidelines was correlated with improved QOL in postoperative prostate cancer survivors.[55]

Few studies have sought to determine the relative effects of cardiovascular and strength training on QOL. In a randomized control trial of prostate cancer patients receiving radiotherapy randomized to a 24 week trial of either strength, aerobic training or usual care, Segal et al found that only strength training improved QOL and fatigue at 24 weeks. In that study, aerobic activity was not correlated with an overall improvement in QOL.[65] However, in this present study strength training was not an independent predictor of good QOL, when controlling for meeting aerobic activity guidelines. One possible reason for this discrepancy is that the study by Segal et al occurred in a population undergoing radiation therapy, while our study focused on *all* cancer survivors, regardless of treatment modality, many of whom were years out from their diagnosis. Radiation may make cardiovascular training more difficult, and the effort required for the increased intensity of activity may be less feasible in this population. Another possible reason that the CDC strength training guidelines were not significantly correlated with improved QOL is that the threshold had not been reached to see an effect. While the CDC guidelines for cardiovascular activity are specific with respect to intensity and duration, the strength-training guidelines only specify 2 times per week.[18] By contrast, the Segal et al strength-training arm consisted of 10 exercises performed for 10-12 reps, 2 sets, 3 times per week. The CDC strength-training guidelines may require a similar titration to intensity and duration that was instituted for cardiovascular guidelines.

On multivariate analysis only higher education was significantly predictive of completing CDC exercise guidelines. The odds ratio of meeting physical activity goals increased almost as a dose response relationship: each higher level of education led to an increase in likelihood of fulfilling CDC guidelines compared with not graduating high school. This relationship has been previously shown in the general population. Highly educated people have a range of healthy behaviors ranging from exercise, to not smoking and moderate alcohol use. Increased feelings of self-efficacy and increased certainty about one's future have been implicated in this trend. Previous studies have found that education level is correlated with physical activity. In a nationwide Dutch sample, Louwman et al found that the increased cancer incidence in less educated groups was partially due to less healthful habits such as smoking and decreased physical activity.[66] Another report from Inoue-Choi et al. found that women who adhered to World Cancer Research Fund recommendations regarding diet, alcohol and physical activity were more likely to have increased education levels. However employment status and insurance level were not assessed in their study, so independence from other socioeconomic factors could not be determined.[67] In their review of socioeconomic disparities of health behaviors, Pampel et al. point to several potential causes for the relationship between exercise and education level: lack of knowledge, lack of efficacy and acculturation.[68] In support of the argument for lack of knowledge, Lyons et al demonstrated that only 63% of older Americans agree that "regular exercise is a highly important part of a healthy lifestyle." The lack of efficacy theory points suggests that even if Americans know that exercise is an important part of a healthy lifestyle, more highly educated people are better able to act on this knowledge.[60] The last theory suggests that higher educated and less

educated populations have different subcultures, and perhaps physical activity is a part of educated culture in a way that it is not for less educated populations.[69,70] While these are potential accounts for our observation that educated cancer survivors are more likely to fulfill CDC physical activity guidelines, these theories have not yet been rigorously tested, and the truth is likely a conglomeration of causes. One way to investigate this further would be a prospective cohort study to evaluate behavior change after an intervention to educate participants about the CDC physical activity guidelines and the role of physical activity in cancer survivorship. Should the issue be about lack of knowledge, there should be uniform improvements in rates of physical activity, regardless of a priori educational or socioeconomic status.

An important advantage of the NHIS is the fact that it is a population-based survey with geographic, socioeconomic and racial diversity weighted to be representative of the United States non-institutionalized population. Thus it is less vulnerable to the selection biases of institution-based surveys. However, because of this structure, this study is subject to important weaknesses as a self-report survey analysis. These include lack of validated information about the cancer pathology, types of treatment and comorbidities. Furthermore, the interviewed population was oversampled for parameters such as race, but not for less common cancers or those with fewer survivors, so the robustness of the statistics for these groups is less than ideal. Thus drawing extensive conclusions regarding particular cancer types has been avoided. Nevertheless, this study provides a valuable overview of adherence to CDC guidelines among American cancer survivors and the effect of this behavior on their QOL.

Aim 3:

Since one of the weaknesses of the NHIS was its lack of data regarding the pathological aspects of the cancer or validated information regarding treatment, a cross-sectional study at the Breast Center – Smilow Cancer Hospital at Yale-New Haven was conducted. In this study, breast cancer survivors were surveyed regarding their QOL and physical activity status and analyzed these with information regarding their cancer pathology and treatment. Twelve percent of breast cancer survivors surveyed completed CDC physical activity guidelines of both aerobic and strength training. The rate of CDC guideline fulfillment was similar to that of the overall compliance of 10.4% in the population-based study using the NHIS. However, it was greater than the proportion of breast cancer survivors who met CDC guidelines, which was 5.2% in that study. Engaging in cardiovascular training was more common than strength training in the cohort of breast cancer patients surveyed at the Breast Center, with 60% of breast cancer survivors meeting cardiovascular guidelines. This was also higher than the 17.4% finding of the study in Aim 2. This discrepancy may be due to the fact that a higher proportion of patients at the Breast Center – Smilow Cancer Hospital had higher education (Master's/Professional/Doctorate) than the general population represented in the NHIS sample (28% vs.13%). Furthermore, the Breast Center – Smilow Cancer Hospital is also the site of several interventions regarding diet and exercise including clinical trials such as LEAN.[71] Indeed, results from both studies in Aim 2 and Aim 3 suggested that education is correlated with physical activity, supporting work done previously.[66-68] Although the majority of breast cancer survivors in this sample met CDC cardiovascular

activity guidelines, only 12% met the CDC requirements of two sessions of strength training per week. This was similar to the 14.3% rate found in the NHIS study.

Most patients in this study reported good QOL, or better, with only 8% reporting fair or poor overall QOL. Similar results were found for physical, mental, and social QOL. These results echoed those of a systematic review of 10 studies regarding the QOL of long-term survivors of breast cancer.[72] In this study fulfilling aerobic exercise requirements was associated with improved QOL, while strength training guidelines were not. This is similar to the results of the study from Aim 2 which also suggested that aerobic, but not strength training, guidelines were associated with improved QOL. The lack of effect on QOL from the strength training guidelines may either be due to the lack of benefit from strength training or due to the inadequacy of the strength training guidelines. In Aim 1, several studies demonstrated that resistance training resulted in improvements in multiple domains of QOL in head and neck cancer survivors. Other studies have shown similar effects for breast cancer survivors and other cancer types.[73-76] However, these studies had investigated full-body weight training regimens with a minimum number of repetitions and sets and at challenging resistance levels, while the CDC guidelines only specify that strength-training exercises should be carried out twice a week. Thus, although our studies require follow-up, they raise the question that the CDC strength training guidelines may not be adequate to improve the QOL of cancer survivors.

The strength of this study is that it accounts for cancer pathology and treatments in providing information about the effect of the CDC physical activity guidelines on QOL of breast cancer patients. The weaknesses, however, are the small sample size, the lack of diversity in the population, and the lack of a standardized QOL survey. However, the

QOL question format allowed for comparability of the data with the NHIS research from Aim 2. Another potential weakness is the lack of comorbidity information that may be obtained in a follow-up study.

Conclusion:

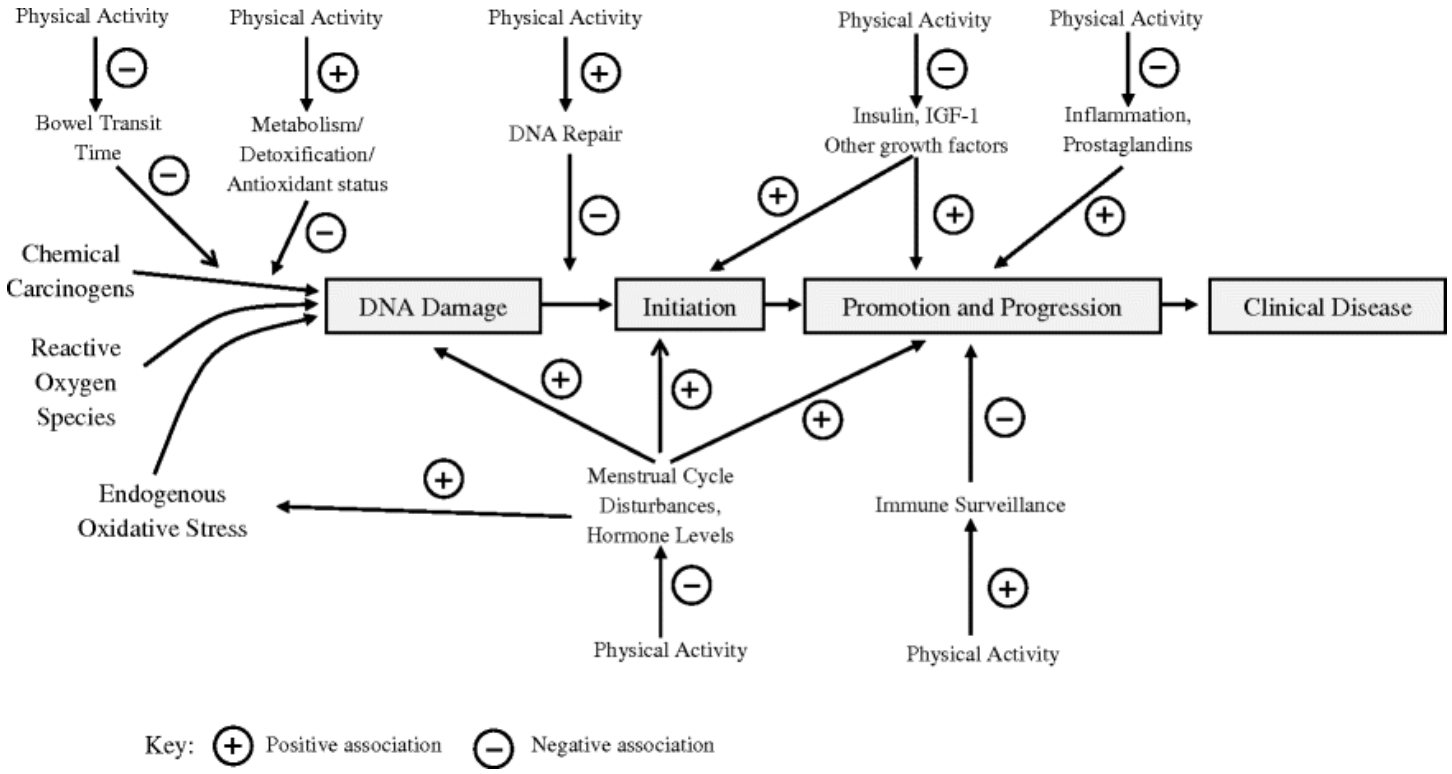
With this thesis, I set out to study the effect of physical activity and the CDC physical activity guidelines on the QOL of cancer survivors. With the systematic review, an understanding of the field in the context of head and neck cancer survivors. Though the data are inconclusive, there seem to be some important benefits in gait speed, muscular strength, and fatigue, with some potential benefits in cognitive function and overall QOL. Next, the effect of the CDC guidelines in improving the QOL of American cancer survivors was investigated. It was found that in a sample of diverse cancer types, geographies, races and educational backgrounds, adherence to the CDC physical activity guidelines was associated with improved overall QOL. However, it was the cardiovascular and not the strength training guidelines that were associated with QOL. Since a weakness of the NHIS was its lack of biological information about the population's cancer status, a study was conducted at the Breast Center – Smilow Cancer Hospital at Yale-New Haven to better understand whether meeting CDC guidelines affects QOL independent of the severity of the cancer type and treatment. It was again found that the cardiovascular and not the strength training guidelines were associated with improved QOL.

With this thesis I demonstrate in my first aim that in a less-studied cancer type both cardiovascular and strength training have a positive influence on multiple domains of

QOL in head and neck cancer survivors. In the subsequent two aims, I demonstrated that CDC strength training guidelines do not correlate with improved QOL, both in a nationwide database that provided insight into national trends as well as a smaller local study that provided more data regarding cancer pathology. Thus, potentially, the CDC strength training guidelines are not meeting their goal of providing sufficient guidance to cancer survivors in improving their QOL. Furthermore, though the CDC cardiovascular activity guidelines are correlated with improved QOL, only 23% of cancer survivors were found to fulfill them in Aim 2. The compliance with the overall guidelines was lower, with only 10.4% fulfilling the full CDC strength and cardiovascular training guidelines in Aim 2 and 12% in Aim 3. A reconsideration of the CDC strength training guidelines is warranted along with increased attention to physical activity in cancer survivors, particularly those who are less educated.

Tables and Figures

Figure 0.1[26] Potential Mechanisms for the Role of Physical Activity in Cancer



Rundle A: Summary of many of the proposed mechanisms linking physical acitivity to lower cancer risk. Physical Activity, Dietary Calorie Restriction, and Cancer, Springer, 2011

Table 0.1[19,20] *Contraindications to Physical Activity*

Absolute	Relative
Recent ECG change or MI	Cardiomyopathy
Unstable angina	Valvular disease
3rd degree heart block	Complex ventricular ectopy
Uncontrolled symptomatic heart failure	Left main coronary stenosis
Uncontrolled hypertension	Electrolyte abnormalities
Uncontrolled metabolic disease (diabetes, thyrotoxicosis, myxedema)	Tachydisrhythmia or bradydisrhythmia
Acute pulmonary embolism or pulmonary infection	Neuromuscular, musculoskeletal or rheumatoid disorder exacerbated by exercise
Suspected or known dissecting aneurysm	Chronic infectious disease (mononucleosis, hepatitis, AIDS)
Acute symptomatic infection with fever, body ache or swollen lymph nodes	

Aim 1

Table 1.1 *Search for Studies on the Effect of Physical Activity and Exercise, on QOL and Survival, in Patients with Head and Neck Cancer (Date of Last Search: Dec 14, 2014)*

Database	Search	Hits
PubMed	(physical[tiab] AND activity[tiab] AND head[tiab] AND neck[tiab] AND cancer[tiab] AND outcomes[tiab]) OR (exercise[tiab] AND head[tiab] AND neck[tiab] AND cancer[tiab] AND outcomes[tiab])OR (physical[tiab] AND activity[tiab] AND head[tiab] AND neck[tiab] AND cancer[tiab] AND quality[tiab] AND life[tiab]) OR (exercise[tiab] AND head[tiab] AND neck[tiab] AND cancer[tiab] AND quality[tiab] AND life[tiab]) OR (physical[tiab] AND activity[tiab] AND head[tiab] AND neck[tiab] AND cancer[tiab] AND survival[tiab]) OR (exercise[tiab] AND head[tiab] AND neck[tiab] AND cancer[tiab] AND survival[tiab])	50
Embase	((physical and activity and head and neck and cancer and outcomes) or (exercise and head and neck and cancer and outcomes) or (physical and activity and head and neck and cancer and quality and life) or (exercise and head and neck and cancer and quality and life) or (physical and activity and head and neck and cancer and survival)).mp. or (exercise and head and neck and cancer and survival).ti,ab.	226
Web of Science	("physical activity" AND "head and neck cancer" AND outcomes) OR (exercise AND "head and neck cancer" AND outcomes) 33 ("physical activity" AND "head and neck cancer" AND “quality of life”) OR (exercise AND "head and neck cancer" AND “quality of life”) 75 ("physical activity" AND "head and neck cancer" AND survival) OR (exercise AND "head and neck cancer" AND survival) 14	85

Figure 1.1 *Flowchart for selection of studies*

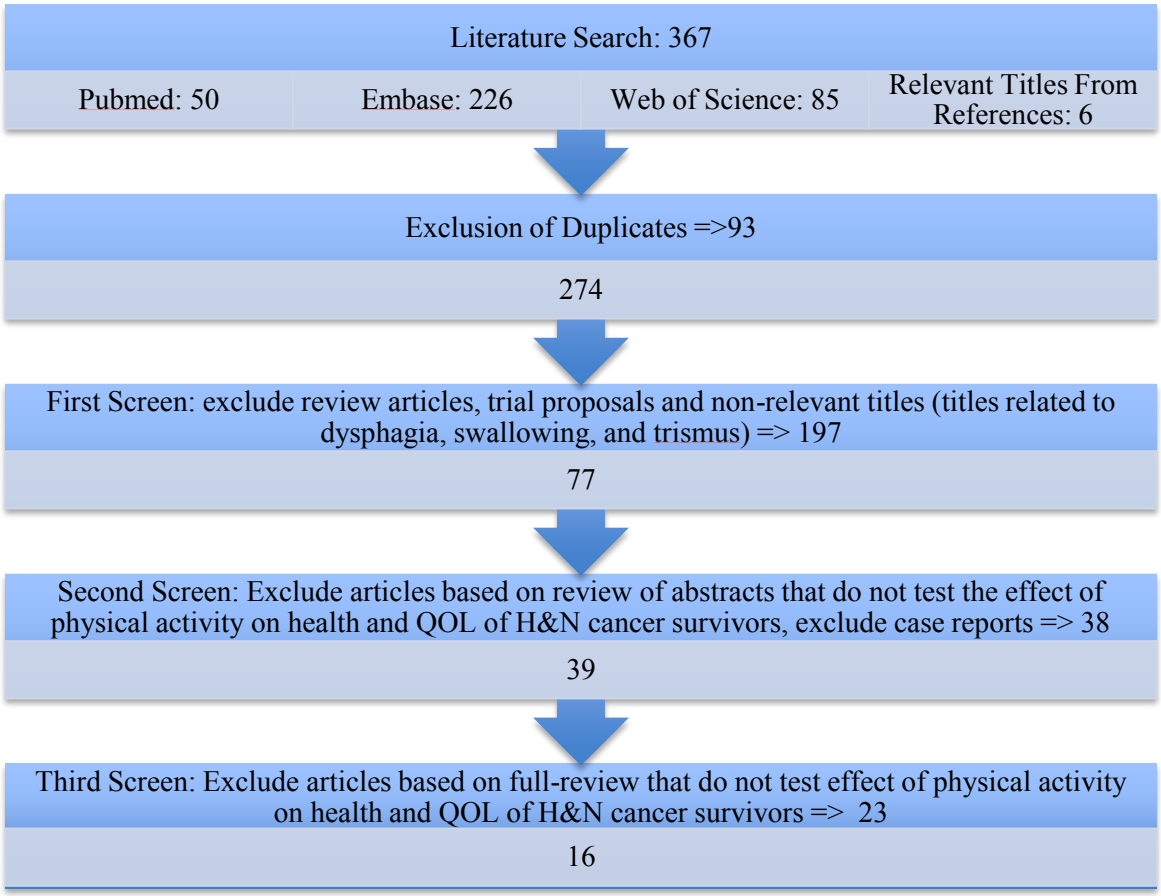


Table 1.2 *Overview of QOL Measures*

QOL Survey	Domains	Length	Scale
EORTC QLQ-C30	Physical, Mental, Emotional, Social Overall	30 questions	0-100
SF-36	Physical, Mental, Emotional, Social	36 questions	0-100
FACT-G	Physical, Social, Emotional, Functional	27 questions	0-112
ESAS	Symptomatic, Emotional	10 questions	0-10

European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ), Short Form 36 (SF-36), Functional Assessment of Cancer Therapy – General (FACT-G), Edmonton Symptom Assessment Scale (ESAS)

Table 1.3 *Assessment and Study Descriptives on the Effect of Physical Activity on Outcomes of Head and Neck Cancer*

Author	**Year**	**(n)**	**Study Design**	**Patients**	**Treatment/ Intervention**	**Outcome**	**Allocation**	**Standard Physical Activity**	**Complete Data**
Aghili	2007	30	Single-arm prospective cohort	Breast and H&N cancer pts s/p rad	Daily 20 min walk, 10 min for frail for 3 weeks, then deep breathing	Fatigue measured by Brief Fatigue Inventory (BFI)	non-random	Yes	100%
Capozzi	2014	21	Single-arm prospective cohort	H&N cancer pts who had or were scheduled to receive rads who had been identified for sx mgmt. using the Edmonton Symptom Assessment System (ESAS)	12-week progressive strength training program: 2 sets x 8-10 reps of 10 exercises of major muscle groups	Anthropometrics, hand grip strength, functional performance, cardiorespiratory fitness with 6 min walk test (6MWT), symptom complaints with Edmonton Symptom Assessment Scale (ESAS)	n/a	Yes	52.4%
Chen	2013	144	Cross-sectional	H&N cancer pts who had completed tx for 3 mo-5yrs	Independent activity measured by Godin exercise questionnaire	Fatigue measured by Fatigue Severity Inventory (FSI)	n/a	No	100%
Eades		27	Single-arm prospective cohort	Squamous Cell Cancer and Adenocarcinoma pts with 2 complex issues like severe pain, drastic weight loss or reduced functional capacity	Semiweekly exercise sessions with home regimen, diet consultation, occupational therapy	Pain, Strength, SOB, Anorexia, Fatigue, Constipation, Insomnia and sleepiness, Nausea and vomiting, Depression, Distress, Functional well being, QOL and sx (ESAS)	n/a	No	71%

Fong	2014	52	Controlled Clinical Trial	Survivors of nasopharyngeal cancer	6 months of Tai Chi Qigong training	Blood flow velocity, arterial resistance, cardiorespiratory function (6MWT),	Non-random	Yes	67.3%
Lonbro	2013	41	RCT	H&N cancer patients after completing radiotherapy	12 wk of progressive resistance training 8-15 reps x 2-3 sets of eg press, knee extension, hamstring curls, chest press, sit ups, back extensions, and lateral pull down followed by 12 wk of independent activity in combination with creatine supplementation	Fatigue, Strength, Physical function, Emotional Function, Cognitive function, QOL	Random	Yes	83%
Lonbro	2013	80	Controlled Clinical Trial	H&N cancer patients after completing radiotherapy and 24 healthy individuals	12 wk of progressive resistance training 8-15 reps x 2-3 sets of eg press, knee extension, hamstring curls, chest press, sit ups, back extensions, and lateral pull down, followed by 12 wk of independent activity	Gait Speed (6MWT), Strength	N/A	Yes	83%
Lonbro	2013	30	RCT	H&N cancer patients after completing radiotherapy	2 groups, one with early exercise in the first 12 wks after completing	Gait Speed (6MWT), Strength	Random	Yes	70%

					radiotherapy followed by 12 wks of independent exercise and the other with the first 12 wks of independent exercise followed by 12 wks of the exercise program. The exercise program consisted of 12 wk of progressive resistance training,, 8-15 reps x 2-3 sets of eg press, knee extension, hamstring curls, chest press, sit ups, back extensions, and lateral pull down				
McNeely	2004	20	RCT	H&N squamous cell cancer patients who had been managed with definitive surgical resection	12 wk of progressive resistance training (6 exercises for scapular stability and upper extremity strength)	Shoulder function, shoulder pain and disability index, QOL (FACT-H&N)	Random	Yes	85%
McNeely	2008	52	RCT	H&N squamous cell cancer patients who had been managed with definitive surgical resection	12 wk of progressive resistance training (6 exercises for scapular stability and upper extremity strength) or 12-week standardized therapeutic exercise	Shoulder function, muscular strength, shoulder pain and disability index, QOL (FACT-An)	Random	Yes	88%

					protocol (ROM/stretching, postural exercise and basic strengthening exercises with light weights				
Rogers	2006	59	Cross-sectional	H&N cancer patients	Independent exercise measured by Godin	QOL measured by FACT-G and FACT-H&N, Fatigue, Functional well being measured by EORTC QLC-C30	N/A	No	91%
Rogers	2013	58	Cross-sectional	H&N cancer patients	Independent exercise measured by Godin	QOL measured by FACT-G and FACT-H&N, Fatigue, Insomnia, Cognitive Function	N/A	No	79%
Samuel	2013	48	RCT	H&N cancer patients during the first wks of radiotherapy onwards	6 wk of individualized and supervised exercise program, brisk walk for 15-20 minutes followed by 8-10 reps x 2-3 sets of resistance exercises for the biceps, triceps, hamstrings and quadriceps.	QOL measured by SF-36, Gait speed (6MWT)	Random	No	90%
Shuman	2012	374	Prospective Cohort	Previously untreated patients with cancer of the upper aerodigestive tract	Independent activity measured by Physical Activity Scale for the Elderly (PASE)	SF-36 bodily pain score	N/A	No	46%

Zhou	2013	12	RCT	H&C cancer patients w/ locally advanced cancer about to begin chemo-radiation	7 wk individualized resistance exercise training followed by 7 wk home program	QOL (SF)-36, Physical Activity Scale for the Elderly (PASE), 6-item Medical Outcomes Study (MOS) Sleep Problem Index	Random	Yes	100%
Duffy	2009	504	Prospective Cohort	H&N cancer patients	Independent activity measured by Physical Activity Scale for the Elderly (PASE)	Survival	N/A	No	81%
6 minute walk test (6MWT), Edmonton symptom assessment scale (ESAS), Physical Activity Scale for the Elderly (PASE), Fatigue Severity Inventory (FSI), Short Form 36 (SF-36), Functional Assessment of Cancer Therapy-General (FACT-G), Functional Assessment of Cancer Therapy-Head and Neck (FACT-H&N), Functional Assessment of Cancer Therapy-Anemia (FACT-An)									

Table 1.4 *Summary of the Effects of Physical Activity on Components of Physical Well Being in Head and Neck Cancer*

Study	Effect
Overall Physical Function	
Lonbro (Rad + Onc)	There was no difference between delayed exercise and early exercise initiation after radiotherapy ($p<0.05$) as both improved overall physical function
Rogers 2013	Physical function did not improve vs control after 6 weeks or 12 week resistance exercise program $p>0.10$
Muscle Strength	
Eades	Exercise program had moderate effect on muscle strength, effect size: 0.8
Lonbro (Rad +Onc)	Both early and delayed exercise program initiation after radiotherapy had significant improvement in lean body mass, knee extension strength, knee flexion strength, arm curl, chair rise, stair climb and gait speed relative to self-chosen exercise $p<0.05$
Lonbro (Healthy)	Knee extension, knee flexion, arm curl, gait speed, chair rise and stair climb were less than healthy controls at baseline $p<0.0001$, but difference was gone after training $p<0.05$
Lonbro (Creatine)	A progressive resistance training program improved arm curl, sit to stand, stair climb, gait speed, knee extension, and knee flexion $p<0.05$
Rogers 2013	Back/leg extension, chair rise and right handgrip did not improve after 12 week resistance exercise program $p>0.10$
Capozzi 2014	Total grip did not improve after resistance exercise intervention ($p=0.31$), but sit to stand results did ($p=0.004$). Chest circumference, waist circumference, hip circumference and bicep circumference did not significantly change during the intervention ($p>0.05$)
McNeely 2004	Shoulder function did not improve with progressive resistance training ($p>0.05$) except for external rotation ($p=0.001$)
McNeely 2008	Muscular strength improved with progressive resistance training program compared to standard physical therapy exercises as measured by seated row, chest press, and endurance test ($p<0.05$ for all)
Gait Speed	
Eades	Exercise program had a moderate effect on gait speed, effect size: 0.8
Samuel	Gait speed improved in those who were in training group $p<0.001$
Lonbro (Rad +Onc)	Both early and delayed exercise had significant improvement in gait speed $p<0.05$
Lonbro (Healthy)	Gait speed was less than healthy controls at baseline $p<0.0001$, but difference was gone after training $p<0.05$
Capozzi 2014	Gait speed improved the 12-week resistance exercise intervention ($p=0.03$)

Fong 2014	Gait speed improved after the 6-month Tai Chi Qigong intervention (p=0.007)
Pain	
Eades	Exercise program had strong effect on pain, effect size: 0.9
Shuman	Those who were physically active (physical activity>121 on PASE) were less likely to have pain p=0.006 on multivariate analysis
Capozzi 2014	Pain was not significantly affected by one exercise session (p=0.21) or by the full 12-week exercise program (p=0.20)
McNeely 2004	Shoulder pain improved with progressive resistance exercise program compared to control (p=0.038)
McNeely 2008	Shoulder pain improved with progressive resistance exercise program compared to standard physical therapy exercises (p=0.004)
Shortness of Breath	
Eades	Exercise program had moderate effect on shortness of breath, Effect size: 0.7
Capozzi 2014	Shortness of breath did not improve after one resistance exercise session (p=0.10) or after the full 12-week exercise program (p=0.24)
Anorexia	
Eades	Exercise program had moderate effect on anorexia, Effect size: 0.7
Capozzi 2014	Appetite did not improve after one resistance exercise session (p=0.66) or after the full 12-week exercise program (p=0.28)
Insomnia	
Eades	Exercise program had moderate effect on insomnia, Effect size: 0.6
Rogers 2008	Level of physical activity was not associated with insomnia, p>0.05
Zhou 2013	Level of sleep disturbance was decreased in the exercise intervention group compared to control, no p value given
Nausea	
Eades	Exercise program had small effect on nausea, Effect size: 0.3
Capozzi 2014	Nausea was not influenced by one resistance exercise session (p=0.45) or by the full 12-week exercise program (p=0.60)
Vomiting	
Eades	Exercise program had small effect on vomiting Effect size: 0.2
Constipation	
Eades	Exercise program had small effect on constipation, Effect size: 0.2
Sleepiness	
Eades	Exercise program had small effect on sleepiness, Effect size: 0.1
Capozzi 2014	Drowsiness was improved by one resistance exercise session (p=0.02), and by the full 12-week exercise program (p=0.04)
Fatigue	
Aghili	Those in the training program had decreased fatigue after 4 weeks of radiotherapy, compared to those in the control group. Median usual fatigue for training group in 1st week: 56% moderate, in 4th week: 38% mild; Median usual fatigue for control group in 1st week: 43% moderate, in 4th week: 57% severe. z=-2.47, p=0.013
Lonbro (Rad +	Both early and delayed exercise after radiotherapy decreased fatigue

Onc)	from baseline at 12 weeks and 24 weeks $p<0.05$. There was no difference between delayed exercise and early exercise, $p>0.05$
Chen	Fatigue varied with exercise intensity $p<0.01$; predictors of fatigue: exercise intensity, depression, age, reconstruction ($r^2=0.26$, $p<0.05$)
Rogers 2013	Resistance training decreased the amount of fatigue experienced by patients undergoing radiotherapy by 8 points at 6 weeks and 3.4 points at 12 weeks, where a 3-point difference is clinically relevant
Rogers 2008	Level of physical activity was not associated with fatigue, $p>0.05$
Rogers 2006	The association between physical activity and decreased fatigue approached significance, $r=-.27$, $p=0.051$
Capozzi 2014	Symptoms of tiredness were improved by one resistance exercise session ($p=0.003$) and by the full 12-week exercise program ($p=0.04$)
McNeely 2008	Fatigue did not improve with the progressive resistance exercise program compared to standard physical therapy exercises ($p=0.54$)
Walking	
Eades	Exercise program had small effect on symptom interference with walking, effect size: 0.4
Physical Well-Being	
Rogers 2013	Resistance training improved physical well-being of patients undergoing radiotherapy by 4 points at 6 weeks and 2.7 points at 12 weeks, where a 1.4-point difference is clinically relevant
Samuel	Training group had same physical well-being after 6 weeks $p=0.478$, but control got worse -5.9, $p=0.064$
Capozzi 2014	Feeling of well-being was improved from one resistance exercise session ($p=0.01$), but not after the full 12-week exercise program ($p=0.16$)
McNeely 2004	Physical well-being was not significantly improved in the progressive resistance training compared with the control ($p=0.67$)

Table 1.5 *Summary of the Effects of Physical Activity on Components of Emotional Well Being in Head and Neck Cancer*

Study	Effect
Worry	
Eades	Exercise program had small effect on worry, Effect size: 0.4
Capozzi 2014	Feeling of anxiety was improved after one resistance exercise session (p=0.01), and its improvement from the full 12-week exercise program approached significance (p=0.06)
Distress/Disability	
Eades	Exercise program had moderate effect on distress, Effect size: 0.7
McNeely 2004	Shoulder disability was not significantly improved in the progressive resistance exercise group compared to control (p=0.11)
McNeely 2008	Shoulder disability improved with progressive resistance exercise program compared to standard physical therapy exercises (p=0.005)
Depression	
Eades	Exercise program had moderate effect on depression, Effect size: 0.6
Rogers 2006	There was no association between depression and physical activity, r=0.10, p=0.50
Capozzi 2014	Symptom of depression was improved after one resistance exercise session (p=0.03) but not by full 12-week exercise program (p=0.11)
Mood	
Eades	Exercise program had small effect on mood, Effect size: 0.4
Emotional Function/Well being	
Lonbro (Rad + Onc)	Early exercise after radiotherapy resulted in improved emotional function relative to baseline at 24 weeks ($p<0.05$), but not at 12 weeks or relative to delayed exercise ($p>0.05$). Delayed exercise did not result in improved emotional function at either time point ($p>0.05$)
Rogers 2013	Resistance training improved emotional well-being of patients undergoing radiotherapy by 0.7 points at 6 weeks and 1.7 points at 12 weeks, where a 0.5-point difference is clinically relevant
McNeely 2004	Emotional well-being was not significantly improved in the progressive resistance exercise group compared to control (p=0.89)
Relations with Others	
Eades	Exercise program had small effect on relations with others, Effect size: 0.3
Social Function/Well being	
Lonbro (Rad +	Early exercise after radiotherapy resulted in improved social

Onc)	function relative to baseline at 24 weeks ($p<0.05$), but not at 12 weeks or relative to delayed exercise ($p>0.05$). Delayed exercise did not result in improved social function at either time point ($p>0.05$)
Rogers 2013	Resistance training did not improve social well-being of patients undergoing radiotherapy at either 6 weeks or 12 weeks, relative to those not in the training program
McNeely 2004	Social/family well-being was not significantly improved in the progressive resistance exercise group compared to control ($p=0.68$)

Table 1.6 *Summary of the Effects of Physical Activity on Components of Functional Well Being in Head and Neck Cancer*

Study	**Effect**
Work	
Eades	Exercise program had small effect on symptom interference with work, Effect size: 0.4
Enjoyment of Life	
Eades	Exercise program had small effect on symptom interference with enjoyment of life, Effect size: 0.3
General Activity	
Eades	Exercise program had small effect on symptom interference with general activity, Effect size: 0.2
Role Function	
Lonbro (Rad and Onc)	Early exercise after radiotherapy resulted in improved role function relative to baseline at 12 weeks ($p<0.05$), but not at 24 weeks or relative to delayed exercise ($p>0.05$). Delayed exercise resulted in improved role function at both time points ($p<0.05$ at 12 weeks and $p<0.001$ at 24 weeks)
Cognitive Function	
Lonbro (Rad and Onc)	Early exercise resulted in improved cognitive function relative to delayed exercise at 12 weeks ($p<0.05$) but there was no longer a significant difference at 24 weeks ($p>0.05$).
Rogers 2008	Level of physical activity was not associated with cognitive function, $p>0.05$
Samuel	Cognitive function of training group improved, $p<0.05$, while that of control group worsened, $p<0.05$
Functional Well Being	
Rogers 2013	Resistance training improved functional well-being of patients undergoing radiotherapy by 2.1 points at 6 weeks and 2.2 points at 12 weeks, where a 1.4-point difference is clinically relevant
Rogers 2006	Level of physical activity was associated with improved functional well-being, $r=0.3$, $p=0.027$
McNeely 2004	Functional well-being was not significantly improved in the progressive resistance training group compared to the control group ($p=0.77$)

Table 1.7 *Summary of the Effects of Physical Activity on QOL Surveys and Overall Survival in Head and Neck Cancer*

Study	**Effect**
QOL	
Eades	Exercise program had moderate effect on QOL, Effect size: 0.8
Lonbro (Rad and Onc)	Early exercise resulted improved overall QOL relative to delayed exercise ($p<0.05$) and from baseline ($p<0.001$) at 12 weeks, however there was no difference at 24 weeks ($p>0.05$), as both had improved QOL from baseline
Zhou 2013	Less decline in QOL (measured with SF-36) was found in exercise group compared to control, no p value given
FACT-G	
Rogers 2006	The relationship between physical activity and overall QOL approached significance, $r=0.25$, $p=0.071$
Rogers 2013	Resistance training improved overall QOL of patients undergoing radiotherapy by 7.4 points at 6 weeks and 6.6 points at 12 weeks, where a 4.4-point difference is clinically relevant
McNeely 2004	Overall QOL did not improve with the progressive resistance exercise program ($p=0.82$)
McNeely 2008	Overall QOL did not improve with the progressive resistance exercise program compared to standard physical therapy exercises ($p=0.09$)
FACT-H&N	
Rogers 2013	Resistance training did not improve H&N-specific QOL of patients undergoing radiotherapy at either 6 weeks or 12 weeks, relative to those not undergoing training
Rogers 2006	The relationship between physical activity and overall QOL approached significance, $r=0.26$, $p=0.064$
McNeely 2004	Head and neck specific QOL did not improve with the progressive resistance exercise program ($p=0.64$)
Survival	
Duffy	Physical activity significantly associated with improved survival on univariate analysis (hazard ratio=0.95; 95% confidence interval: 0.93-0.97; $p<0.01$), but not multivariate (hazard ratio=0.98; 95% confidence interval: 0.95-1.0; $p=0.085$)

Aim 2

Table 2.1 *Sociodemographic factors associated meeting CDC overall activity guidelines*

Characteristic	Weighted Sample	Univariate		Multivariate	
		%	P-value*	OR (95% CI)†	P-valu
Total	19221052	10.41	n/a	n/a	n/a
Sex			0.081	n/a	n/a
Male	8470262	11.9			
Female	10970790	9.3			
Age (yrs)			<0.001		0.74
<40	2426521	16.1		Referent	
40-65	8460643	13.5		0.92 (0.49-1.70)	
>65	8553888	5.7		0.69 (0.26-1.79)	
Race and ethnicity			0.002		0.26
Hispanic	964584	8.3		1.18 (0.48-2.93)	
White	16762786	11.1		Referent	
Black	1280981	4.0		0.49 (0.19-1.28)	
Asian	282542	4.1		0.39 (0.08-1.90)	
Other	150159	13.7		2.99 (0.54-16.65)	
Education			<0.001		<0.001
Less than high school	2506449	2.7		Referent	
High school graduate	5281065	4.5		2.35 (0.70-7.82)	
Some college	5784389	9.8		3.92 (1.21-12.69)	
Bachelor's degree	3249763	17.0		8.03 (2.45-26.34)	
Master's degree	1726707	21.2		9.72 (2.89-32.70)	
Professional degree	812129	29.1		14.25 (3.58-56.70)	
Insurance			<0.001		0.75
Not Covered	1151645	13.6		Referent	
Medicare	9775390	5.9		0.88 (0.28-2.77)	
Medicaid	738079	6.6		0.76 (0.21-2.77)	
Military	513023	16.7		2.12 (0.48-9.32)	
Private	6972756	15.8		1.05 (0.42-2.64)	
Marital Status			<0.001		0.11
Married	11693965	11.4		Referent	
Widowed	2698797	3.3		0.42 (0.16-1.10)	
Divorced/Separated	2898668	10.7		0.99 (0.48-2.03)	
Never Married	1353063	15.3		1.58 (0.79-3.16)	
Living with Partner	785857	11.0		0.56 (0.17-1.84)	

Employment Status			<0.001		0.61
Working	6991478	15.5		Referent	
Looking for Work	597082	15.1		1.06 (0.42-2.72)	
Not working and not looking	11271308	7.1		0.76 (0.42-1.37)	
Type of Cancer			<0.001		0.07
Head and Neck	255421	10.6		Referent	
Breast	2718868	5.2		0.40 (0.08-1.93)	
Cervical	1154690	18.1		1.41 (0.31-6.31)	
Ovarian	390509	8.3		0.75 (0.11-5.33)	
Uterine	762658	7.5		0.61 (0.13-2.83)	
Prostate	2060398	8.4		0.62 (0.13-2.99)	
Bladder	443021	6.8		0.59 (0.07-4.69)	
Kidney	287839	4.5		0.31 (0.03-3.58)	
Thyroid	434636	13.1		0.87 (0.16-4.76)	
Colorectal	1042946	4.3		0.29 (0.04-2.17)	
Testicular	205634	20.9		1.06 (0.17-6.56)	
Leukemia/Lymphoma	925057	8.1		0.47 (0.10-2.24)	
Lung	440424	1.6		0.18 (0.02-2.07)	
Melanoma	1348038	21.0		1.32 (0.33-5.18)	
Other	633918	4.1		0.22 (0.03-1.61)	

Table 2.2 *Sociodemographic factors associated with meeting CDC cardiovascular activity guidelines*

Characteristic	Univariate		Multivariate	
	%	P-value	OR (95% CI)	P-value
Total	23.0	n/a	n/a	n/a
Sex		<0.001		0.056
Male	27.0		Referent	
Female	19.9		0.59 (0.34-1.01)	
Age (yrs)		<0.001		<0.001
<40	38.6		Referent	
40-65	27.2		0.37 (0.23-0.60)	
>65	14.4		0.44 (0.21-0.94)	
Race and ethnicity		<0.001		0.020
Hispanic	14.8		0.55 (0.26-1.15)	
White	24.6		Referent	
Black	11.7		0.53 (0.29-0.98)	
Asian	7.2		0.24 (0.07-0.84)	
Other	22.6		1.77 (0.44-7.05)	
Education		<0.001		<0.001
Less than high school	8.3		Referent	
High school graduate	15.6		1.65 (0.93-2.92)	
Some college	24.0		2.48 (1.45-4.26)	
Bachelor's degree	32.1		3.80 (2.14-6.76)	
Master's degree	35.6		4.94 (2.63-9.27)	
Professional degree	48.6		5.44 (2.30-12.91)	
Insurance		<0.001		0.202
Not Covered	30.4		Referent	
Medicare	14.2		0.45 (0.19-1.05)	
Medicaid	18.2		0.58 (0.23-1.45)	
Military	29.0		1.01 (0.31-3.33)	
Private	33.7		0.91 (0.50-1.68)	

Marital Status		<0.001		0.463
Married	25.4		Referent	
Widowed	10.9		0.71 (0.42-1.20)	
Divorced/Separated	22.0		0.84 (0.50-1.40)	
Never Married	27.9		0.88 (0.51-1.52)	
Living with Partner	22.6		0.45 (0.17-1.24)	
Employment Status		<0.001		0.441
Working	32.4		Referent	
Looking for Work	36.0		1.54 (0.71-3.31)	
Neither working nor looking	16.4		0.92 (0.63-1.36)	
Type of Cancer		<0.001		<0.001
Head and Neck	16.1		Referent	
Breast	17.4		1.33 (0.39-4.62)	
Cervical	40.8		2.80 (0.76-10.33)	
Ovarian	17.5			
Uterine	14.6		1.17 (0.23-5.94)	
Prostate	24.7		0.97 (0.24-3.97)	
Bladder	21.3		1.16 (0.33-4.08)	
Kidney	9.1		1.10 (0.25-4.90)	
Thyroid	27.9		0.35 (0.07-1.92)	
Colorectal	9.1		1.39 (0.36-5.30)	
Testicular	33.8		0.46 (0.12-1.77)	
Leukemia/Lymphoma	14.1		1.20 (0.26-5.59)	
Lung	5.7		0.41 (0.12-1.49)	
Melanoma	40.3		0.39 (0.08-1.94)	
Other	12.8		2.10 (0.63-6.97)	

Table 2.3 *Sociodemographic factors associated with meeting CDC strength training guidelines*

Characteristic	Univariate		Multivariate	
	%	P-value	OR (95% CI)	P-value
Total	19.9	n/a	n/a	n/a
Sex		0.025		0.19
Male	22.5		Referent	
Female	17.9		0.83 (0.63-1.09)	
Age (yrs)		0.002		0.28
<40	25.7		Referent	
40-65	21.6		0.74 (0.49-1.12)	
>65	16.6		0.67 (0.39-1.14)	
Race and ethnicity		0.002		0.08
Hispanic	19.8		1.12 (0.62-2.02)	
White	20.8		Ref	
Black	10.8		0.57 (0.31-1.03)	
Asian	9.4		0.33 (0.11-0.94)	
Other	17.6		1.11 (0.24-5.16)	
Education		<0.001		<0.001
Less than high school	8.9		Referent	
High school graduate	11.1		1.23 (0.68-2.23)	
Some college	21.3		2.70 (1.58-4.62)	
Bachelor's degree	27.1		3.52 (1.97-6.28)	
Master's degree	36.0		5.55 (3.09-9.95)	
Professional degree	37.8		5.78 (2.74-	
Insurance		0.012		0.99
Not Covered	19.4		Referent	
Medicare	16.8		0.91 (0.45-1.85)	
Medicaid	14.7		0.86 (0.34-2.17)	
Military	25.3		1.03 (0.36-2.93)	
Private	24.7		0.98 (0.55-1.76)	
Marital Status		0.001		0.53
Married	21.3		Referent	
Widowed	12.5		0.77 (0.52-1.13)	
Divorced/Separated	20.3		0.92 (0.66-1.30)	
Never Married	22.1		0.96 (0.58-1.60)	
Living with Partner	18.9		0.68 (0.34-1.36)	

Employment Status		0.008		0.47
Working	23.7		Referent	
Looking for Work	27.7		1.48 (0.78-2.83)	
Neither working nor looking	17.1		0.99 (0.69-1.42)	
Type of Cancer		0.249	n/a	n/a
Head and Neck	21.1			
Breast	14.3			
Cervical	25.4			
Ovarian	16.0			
Uterine	14.4			
Prostate	20.3			
Bladder	15.9			
Kidney	9.9			
Thyroid	20.6			
Colorectal	11.9			
Testicular	26.4			
Leukemia/Lymphoma	21.4			
Lung	13.3			
Melanoma	24.8			
Other	19.6			

Table 2.4 *Univariate Analysis of QOL and Meeting CDC Guidelines*

Characteristic	Cardio		P Value	Strength		P Value	All Guidelines		P Value
	Yes	No		Yes	No		Yes	No	
Fatigue in Past 7 D			<0.001			<0.001			<0.001
None	34.0	26.5		32.9	27.1		33.4	27.7	
Mild	41.3	37.9		43.4	37.6		42.2	38.3	
Moderate	20.0	25.7		18.4	25.8		19.3	24.9	
Severe	4.3	7.4		4.4	7.2		5.2	6.8	
Very Severe	0.4	2.6		0.9	2.4		0.0	2.3	
Reported QOL			<0.001			<0.001			<0.001
Excellent	47.5	25.0		41.8	27.4		47.8	28.3	
Very good	30.9	33.0		34.5	32.1		35.0	32.2	
Good	16.9	27.4		16.6	27.0		13.7	26.3	
Fair	4.4	11.0		5.2	10.5		3.0	10.2	
Poor	0.3	3.5		1.9	3.0		0.5	3.0	
Physical Health			<0.001			<0.001			<0.001
Excellent	28.2	9.8		26.8	11.0		35.2	11.7	
Very good	39.1	27.4		36.9	28.5		38.3	29.2	
Good	26.3	35.1		23.4	35.5		20.4	34.5	
Fair	5.3	19.3		9.5	17.6		4.3	17.4	
Poor	1.2	8.4		3.4	7.5		1.9	7.2	
Mental Health			<0.001			<0.001			<0.001
Excellent	40.4	24.2		37.2	25.7		41.3	26.5	
Very good	37.8	32.4		37.4	32.8		41.4	32.8	
Good	15.9	30.1		16.0	29.5		12.0	28.5	
Fair	4.9	10.2		8.0	9.1		4.7	9.4	
Poor	1.0	3.1		1.4	2.9		0.6	2.9	

Characteristic	Cardio		P Value	Strength		P Value	All Guidelines		P Value
	Yes	No		Yes	No		Yes	No	
Social Relationships			<0.001			<0.001			<0.001
Excellent									
Very good	34.4	22.7		33.6	23.4		37.7	24.0	
Good	35.3	29.4		35.3	29.7		37.5	30.0	
Fair	24.3	33.0		20.6	33.5		18.0	32.4	
Poor	5.2	9.1		6.9	8.5		5.2	8.5	
	0.7	5.8		3.6	4.9		1.6	5.0	

Table 2.5 *Multivariate Analysis of Factors Predicting QOL*

Characteristic	Good QOL	
	OR (95% CI)	P Value
Sex		0.344
Male	Referent	
Female	1.32 (0.74-2.36)	
Age (yrs)		0.012
<40	0.50 (0.20-1.23)	
40-65	0.39 (0.21-0.73)	
>65	Referent	
Race and ethnicity		0.344
Hispanic	1.06 (0.58-1.91)	
White	Referent	
Black	0.94 (0.59-1.50)	
Asian	0.40 (0.16-1.01)	
Other	2.12 (0.33-13.71)	
Education		<0.001
Less than high school	Referent	
High school graduate	1.23 (0.78-1.96)	
Some college	2.50 (1.50-4.17)	
Bachelor's degree	7.58 (3.48-16.54)	
Master's degree	2.94 (0.96-9.03)	
Professional degree	3.39 (0.71-16.29)	
Insurance		0.026
Not Covered	1.77 (0.77-4.06)	
Medicare	1.27 (0.58-2.82)	
Medicaid	Referent	
Military	0.77 (0.23-2.59)	
Private	2.95 (1.19-7.31)	
Marital Status		0.043
Married	Referent	
Widowed	0.88 (0.51-1.52)	
Divorced/Separated	0.44 (0.27-0.74)	
Never Married	0.71 (0.33-1.52)	
Living with Partner	0.82 (0.32-2.13)	

Characteristic	Good QOL	
	OR (95% CI)	P Value
Employment Status		0.001
Working	Referent	
Looking for Work	0.59 (0.16-2.16)	
Not working and not looking	0.41 (0.25-0.67)	
Type of Cancer		0.406
Head and Neck	Referent	
Breast	1.30 (0.40-4.24)	
Cervix	1.21 (0.31-4.63)	
Ovary	0.54 (0.11-2.69)	
Uterus	1.28 (0.33-5.02)	
Prostate	1.52 (0.41-5.65)	
Bladder	1.10 (0.20-6.15)	
Kidney	1.01 (0.20-5.09)	
Thyroid	0.52 (0.10-2.69)	
Colorectal	1.05 (0.32-3.42)	
Testicular	2.63 (0.22-31.40)	
Lymphoma/Leukemia	0.81 (0.22-2.92)	
Lung	0.39 (0.10-1.54)	
Melanoma	1.13 (0.32-4.04)	
Other	0.78 (0.19-3.23)	
All Guidelines		0.021
Yes	4.42 (1.26-15.49)	
No	Referent	

Table 2.6 *Multivariate Analysis of QOL and Activity Subcategories*

Characteristic	Good QOL	
	OR (95% CI)	P Value
Cardiovascular Guidelines Yes No	3.63 (1.77-7.43) Referent	<0.001
Strength Guidelines Yes No	0.88 (0.48-1.62) Referent	0.683

Aim 3

Table 3.1 *Background table of sample*

Characteristic	%	Characteristic	%
Sociodemographic Factors			
Sex		Age	n/a
Male	0		
Female	100		
Marital Status		Financial problems due to cancer	
Married/Domestic partner	72	Not At All	52
Widowed	14	A Little	20
Divorced/Separated	12	Some	20
Never Married	2	A Lot	8
Race and ethnicity		Education	
White	84	< or High school graduate	26
Black	14	Some college or Bachelor's	46
Other	2	Master's/Professional/Doctorate	28
Insurance			
Medicare	28		
Medicaid	8		
Private	64		
Breast Cancer Variables			
Grade		Margins	
Well Differentiated	34	Positive	10.6
Moderately Differentiated	57	Negative	89.4
Poorly Differentiated	9		
Lymphovascular Invasion		Progesterone Receptor	
Yes	17.8	Positive	82.9
No	82.2	Negative	17.1
Estrogen Receptor		Radiation Therapy	
Positive	88.6	Yes	79.2
Negative	11.4	No	20.8
Chemotherapy		Tamoxifen	
Yes	31.9	Yes	36.2
No	68.1	No	63.8

Herceptin Yes No	 6.5 93.5	Nodal surgery Yes No	 71 29
Size of invasive lesion (mean)	1.9	Time Since Surgery (mean)	2.4 years
Physical Activity Guidelines			
Strength/Overall CDC Guidelines Yes No	 88 12	Aerobic guidelines Yes No	 60 40

Table 3.2 *Univariate analysis of meeting CDC physical activity guidelines*

Characteristic and % meeting guidelines	Meet Guidelines	Do Not Meet Guidelines	P-value
Sociodemographic Factors			
Mean Age	59.4	60.9	0.298
Education			0.059
High School Grad or less	0%	100%	
Bachelor's/Assoc/Some college	8.7%	91.3%	
Higher Degree	28.6%	71.4%	
Race and ethnicity			0.918
Black	14.3%	85.7%	
White	11.9%	88.1%	
Other	0%	100%	
Insurance			0.534
Medicaid	0%	100%	
Medicare	7.1%	92.9%	
Private	15.6%	84.4%	
Marital Status			0.748
Divorced/sep	16.7%	83.3%	
Living w/ partner	0%	100%	
Married/dom partner	15.2%	84.8%	
Never married	0%	100%	
Widowed	0%	100%	
Worry about recurrence			0.539
Never	0%	100%	
Often	14.3%	85.7%	
Rarely	6.2%	93.8%	
Sometimes	19%	81%	
Always	0.0%	100%	
Likelihood of cancer return			0.378
Fairly high	0%	100%	
Moderate	22.2%	77.8%	
Fairly low	20%	80%	
Very low	4.3%	95.7%	
Financial problems due to cancer			0.098
Not at all	23.1%	76.9%	
A little	0%	100%	
Some	0%	100%	

A lot	0%	100%	
Breast Cancer Variables			
Grade 1 2 3	 25% 6.5% 0%	 75% 93.5% 0%	0.281
Progesterone Receptor Negative Positive	 16.7% 10.3%	 83.3% 89.7%	0.029
Lymph node surgery Yes No	 0% 16.2%	 100% 83.8%	<0.001
Nodal Status Positive Negative Missing	 0% 16.7% 8.3%	 100% 83.3% 91.7%	0.260
Mean time Since Surgery	2.60 yrs	2.41 yrs	0.792
Estrogen Receptor: Negative Positive	 0% 12.9%	 87.1% 86.7%	0.001
Mean size of invasive lesion	2.92 cm	1.81 cm	0.069
Margins Positive Negative	 20% 11.9%	 80% 88.1%	0.109
Lymphovascular Invasion Yes No	 0% 13.5%	 100% 86.5%	0.020
Chemotherapy Yes No	 6.7% 15.6%	 93.3% 84.4%	0.391
Herceptin Yes	 0%	 100%	0.488

No	14%	86%	
Radiation Therapy Yes No	 15.8% 0%	 84.2% 100%	 0.179
Tamoxifen Yes No	 5.9% 16.7%	 95.1% 83.3%	 0.287

Table 3.2 *Univariate analysis of meeting CDC strength training guidelines*

Characteristic and % meeting guidelines	Meet Guidelines	Do Not Meet Guidelines	P-value
Sociodemographic Factors			
Age (mean)	59.4	60.9	0.298
Education			0.059
High School Grad or less	0.0%	100.0%	
B.A., Assoc/Some college	8.7%	91.3%	
Higher Degree	28.6%	71.4%	
Race and ethnicity			0.918
Black	14.3%	85.7%	
White	11.9%	88.1%	
Other	0.0%	100.0%	
Insurance			0.534
Medicaid	0.0%	100.0%	
Medicare	7.1%	92.9%	
Private	15.6%	84.4%	
Marital Status			0.748
Divorced/sep	16.7%	83.3%	
Living w/ partner	0.0%	100.0%	
Married/dom partner	15.2%	84.8%	
Never married	0.0%	100.0%	
Widowed	0.0%	100.0%	
Worry about recurrence			0.539
Never	0.0%	100.0%	
Often	14.3%	85.7%	
Rarely	6.2%	93.8%	
Sometimes	19.0%	81.0%	
Always	0.0%	100.0%	
Likelihood of cancer return			0.378
Fairly high	0.0%	100.0%	
Moderate	22.2%	77.8%	
Fairly low	20.0%	80.0%	
Very low	4.3%	95.7%	
Financial problems due to cancer			0.098
Not at all	23.1%	76.9%	
A little	0.0%	100.0%	
Some	0.0%	100.0%	

A lot	0.0%	100.0%	
Breast Cancer Variables			
Grade 1 2 3	 25.0% 6.5% 0.0%	 75.0% 93.5% 0.0%	0.281
Progesterone Receptor Negative Positive	 16.7% 10.3%	 83.3% 89.7%	0.029
Lymph node surgery Yes No	 0.0% 16.2%	 100.0% 83.8%	<0.001
Nodal Status Positive Negative Missing	 0.0% 16.7% 8.3%	 100.0% 83.3% 91.7%	0.260
Mean time Since Surgery	2.60 yrs	2.41 yrs	0.792
Estrogen Receptor: Negative Positive	 0.0% 12.9%	 87.1% 86.7%	0.001
Mean size of invasive lesion	2.92 cm	1.81 cm	0.069
Margins Positive Negative	 20.0% 11.9%	 80.0% 88.1%	0.109
Lymphovascular Invasion Yes No	 0.0% 13.5%	 100.0% 86.5%	0.020
Chemotherapy Yes No	 6.7% 15.6%	 93.3% 84.4%	0.391
Herceptin Yes	 0%	 100%	0.488

No	14.0%	86.0%	
Radiation Therapy Yes No	 15.8% 0.0%	 84.2% 100.0%	 0.179
Tamoxifen Yes No	 5.9% 16.7%	 95.1% 83.3%	 0.287

Table 3.3 *Univariate analysis of meeting CDC aerobic activity guidelines*

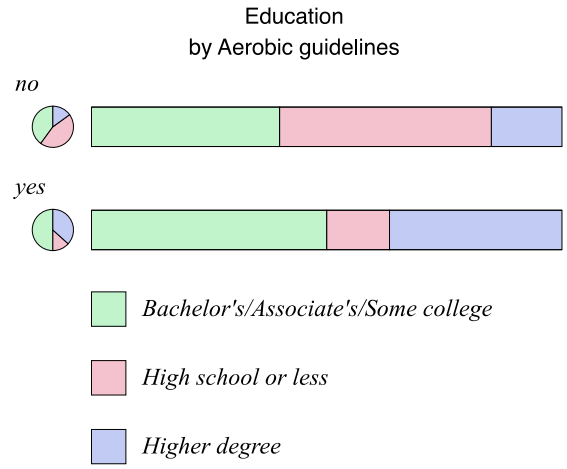
Characteristic	Met Guidelines	Did Not Meet Guidelines	P-value
Sociodemographic Factors			
Mean age	59.2 yrs	63.1 yrs	0.276
Education			0.032
High School or Less	30.8%	69.2%	
Bachelor's/Assoc/Some college	65.2%	34.8%	
Higher degree	78.6%	21.4%	
Race and ethnicity			0.262
Black	42.9%	57.1%	
White	64.3%	35.7%	
Other	0.0%	100.0%	
Marital Status			0.701
Divorced/Sep	50.0%	50.0%	
Living w/ partner	33.3%	66.7%	
Married/domestic partner	60.6%	39.4%	
Never married	100.0%	0.0%	
Widowed	71.4%	28.6%	
Insurance			0.014
Medicaid	25.0%	75.0%	
Medicare	35.7%	64.3%	
Private	75.0%	25.0%	
Likelihood of cancer return			0.763
Very low	56.5%	43.5%	
Fairly low	53.3%	46.7%	
Moderate	66.7%	33.3%	
Fairly high	100.0%	0.0%	
Very high	0.0%	0.0%	
Worry about recurrence			0.245
Never	20.0%	80.0%	
Rarely	56.2%	43.8%	
Sometimes	66.7%	33.3%	
Often	71.4%	28.6%	
Always	0.0%	0.0%	
Financial problems due to cancer			0.003
Not at all	73.1%	26.9%	
A little	80.0%	20.0%	
Some	10.0%	90.0%	
A lot	50.0%	50.0%	

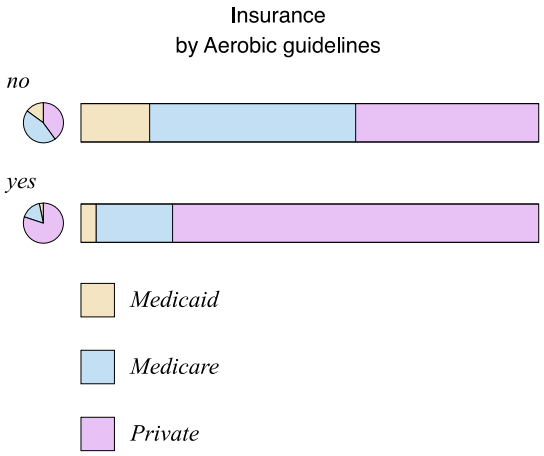
Breast Cancer Variables			
Margins Positive Negative	 60.0% 57.1%	 40.0% 42.9%	0.903
Grade 1 2 3	 68.8% 51.6% 0.0%	 31.2% 48.4% 0.0%	0.133
Estrogen Receptor Positive Negative	 61.3% 25.0%	 38.7% 75.0%	0.167
Progesterone Receptor Positive Negative	 58.6% 50.0%	 41.4% 50.0%	0.698
Lymphovascular Invasion Yes No	 62.5% 56.8%	 37.5% 43.2%	0.766
Mean time Since Surgery	2.38 yrs	2.51 yrs	0.751
Lymph node surgery Yes No	 0.0% 56.8%	 100.0% 43.2%	0.526
Nodal Status Postive Negative Missing	 62.5% 60.0% 58.3%	 37.5% 40.0% 41.7%	0.975
Mean size of invasive lesion	1.7 cm	2.3 cm	0.267
Chemotherapy Yes No	 52.5% 62.5%	 46.7% 37.5%	0.551
Radiation Therapy Yes No	 63.2% 50.0%	 36.8% 50.0%	0.449

Tamoxifen Yes No	 70.6% 53.3%	 29.4% 46.7%	0.247
Herceptin Yes No	 66.7% 58.1%	 33.3% 41.9%	0.772

Figure 3.1 *Breakdown of significant factors in completion of aerobic activity guidelines*

"yes"= completed guidelines "no"= did not complete guidelines





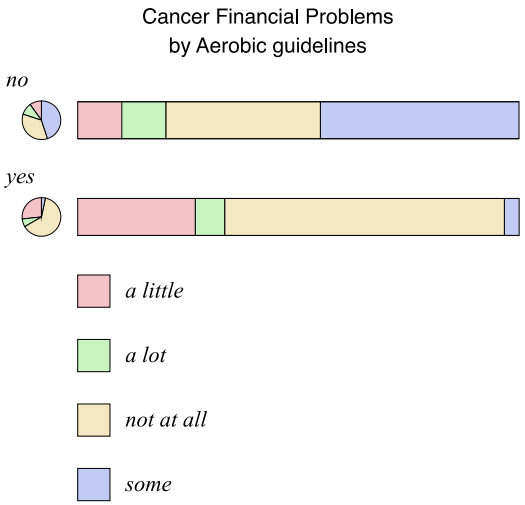


Figure 3.2 *Distribution of QOL of Sample*

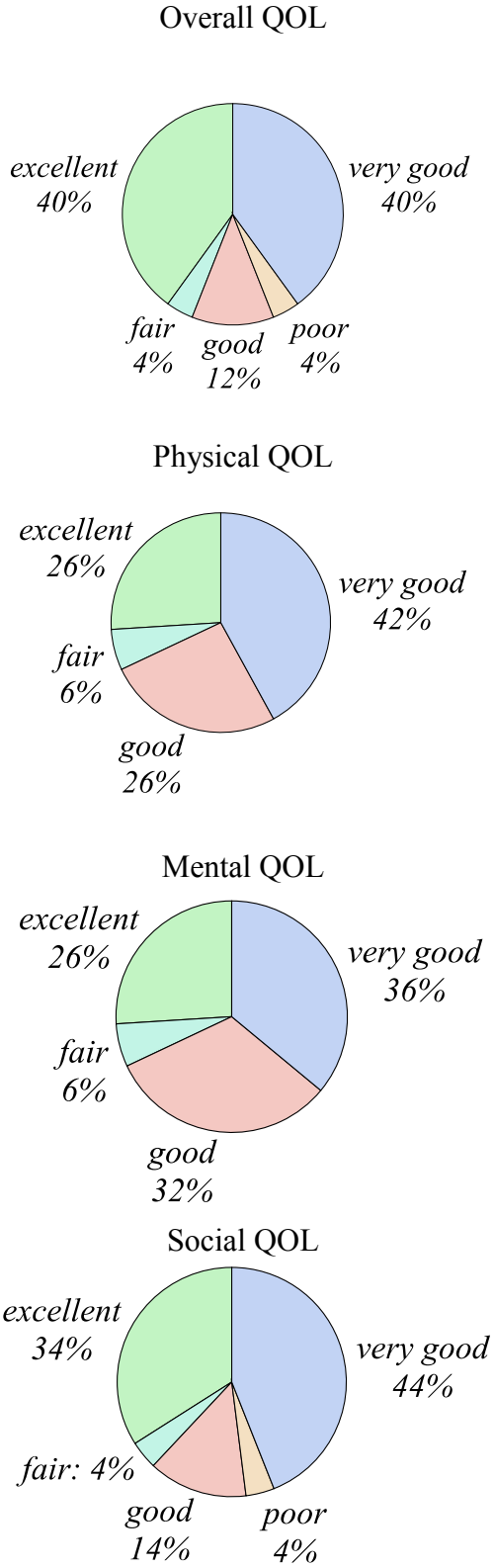


Table 3.4 *Univariate Analysis of Overall QOL*

Characteristic	Excellent	V. Good	Good	Fair	Poor	P-value
Sociodemographic Factors						
Mean age	62.6 yrs	58.1 yrs	69.0 yrs	59.5 yrs	48 yrs	0.309
Race						0.610
Black	28.6%	28.6%	28.6%	14.3%	0.0%	
White	42.9%	40.5%	9.5%	2.4%	4.8%	
Other	0.0%	100.0%	0.0%	0.0%	0.0%	
Education						0.019
HS grad or less	23.1%	38.5%	15.4%	7.7%	15.4%	
BA/Assoc/Some college	26.1%	56.5%	13.0%	4.3%	0.0%	
Higher Degree	78.6%	14.3%	7.1%	0.0%	0.0%	
Insurance						<0.001
Medicaid	0.0%	50.0%	0.0%	0.0%	50.0%	
Medicare	50.0%	28.6%	21.4%	0.0%	0.0%	
Private	40.6%	43.8%	9.4%	6.2%	0.0%	
Marital Status						0.535
Divorced/Sep	50.0%	50.0%	0.0%	0.0%	0.0%	
Living w/ partner	0.0%	33.3%	33.3%	0.0%	33.3%	
Married/Dom partner	45.5%	36.4%	12.1%	3.0%	3.0%	
Never married	0.0%	100.0%	0.0%	0.0%	0.0%	
Widowed	28.6%	42.9%	14.3%	14.3%	0.0%	

Financial problems due to cancer						0.013
Not at all	57.7	30.8%	20.0%	0.0%	0.0%	
A little	40.0%	40.0%	0.0%	0.0%	0.0%	
Some	0.0%	50.0%	11.5%	20.0%	20.0%	
A lot	25.0%	75.0%	10.0%	0.0%	0.0%	
Likelihood of cancer return						0.344
Very low	52.2%	34.8%	13.0%	0.0%	0.0%	
Fairly Low	46.7%	26.7%	6.7%	6.7%	13.3%	
Moderate	11.1%	55.6%	22.2%	11.1%	0.0%	
Fairly High	0.0%	100.0%	0.0%	0.0%	0.0%	
Very High	0.0%	0.0%	0.0%	0.0%	0.0%	
Worry about recurrence						0.060
Never	60.0%	40.0%	0.0%	0.0%	0.0%	
Rarely	62.5%	18.8%	12.5%	6.2%	0.0%	
Sometimes	28.6%	52.4%	14.3%	4.8%	0.0%	
Often	14.3%	42.9%	14.3%	0.0%	28.6%	

Breast Cancer Variables

Characteristic	Excellent	V. Good	Good	Fair	Poor	P-value
Grade						0.071
1	50.0%	43.8%	0.0%	6.2%	0.0%	
2	38.7%	32.3%	19.4%	3.2%	6.5%	
3	0.0%	0.0%	0.0%	0.0%	0.0%	
Mean size of invasive lesion (cm)	2.32	1.22	2.08	2.10	2.80	0.588

Margins						0.608
Positive	100.0%	0.0%	0.0%	0.0%	0.0%	
Negative	35.7%	40.5%	14.3%	4.8%	4.8%	
Lymphovascular Invasion						0.270
Yes	25.0%	25.0%	50.0%	0.0%	0.0%	
No	45.9%	37.8%	5.4%	5.4%	5.4%	
Progesterone Receptor						0.658
Positive	44.8%	34.5%	13.8%	0.0%	6.9%	
Negative	33.3%	16.7%	16.7%	33.3%	0.0%	
Estrogen Receptor						0.445
Positive	48.4%	32.3%	12.9%	0.0%	6.5%	
Negative	0.0%	25.0%	25.0%	50.0%	0.0%	
Chemotherapy						0.006
Yes	60.0%	6.7%	20.0%	13.3%	0.0%	
No	34.4%	53.1%	6.2%	0.0%	6.2%	
Herceptin						0.073
Yes	33.3%	0.0%	66.7%	0.0%	0.0%	
No	44.2%	37.2%	9.3%	4.7%	4.7%	
Radiation Therapy						0.071
Yes	44.7%	36.8%	13.2%	5.3%	0.0%	
No	30.0%	40.0%	10.0%	0.0%	20.0%	
Tamoxifen						0.254
Yes	41.2%	52.9%	5.9%	0.0%	0.0%	
No	43.3%	26.7%	16.7%	6.7%	6.7%	

Mean time Since Surgery (years)	2.44	2.42	0.0%	2.74	0.0%	0.752
Lymph node surgery Yes No	 0.0% 43.2%	 0.0% 35.1%	 0.0% 16.2%	 100.0% 0.0%	 0.0% 5.4%	0.661
Nodal Status Positive Negative Missing	 62.5% 40.0% 25.0%	 0.0% 46.7% 50%	 12.5% 6.7% 25%	 0.0% 6.7% 0.0%	 25.0% 0.0% 0.0%	0.013
Physical Activity Guidelines						
Overall CDC guidelines Yes No	 66.7% 36.4%	 33.3% 40.9%	 0.0% 13.6%	 0.0% 4.5%	 0.0% 4.5%	0.618
Aerobic guidelines Yes No	 46.7% 30.0%	 46.7% 30.0%	 6.7% 20%	 0.0% 10.0%	 0.0% 10.0%	0.051
Strength guidelines Yes No	 66.7% 36.4%	 33.3% 40.9%	 0.0% 13.6%	 0.0% 4.5%	 0.0% 4.5%	0.618

Appendix

Physical activity and quality of life survey

Please answer the following questions by placing an X next to your answer.

How old are you? _____ years

What is your race?
___ Caucasian
___ Black/African American
___ American Indian or Alaskan Native
___ Asian
___ Other

What is your marital status?
___ married
___ widowed _
__ divorced
___ separated _
__ never married _
__ living with partner

What is the highest level of school you have completed or the highest degree you have received?
___ high school or less
___ high school graduate
___ some college / associate degree
___ bachelor's degree (example: BA, AB, BS, BBA)
___ master's degree (example: MA, MS, MEng, MEd, MBA)
___ graduate or professional degree (example: MD, PhD, DDS, DVM, JD)

Please choose the category that best describes your sexual orientation.
___ straight ___ lesbian ___ bisexual ___ other

What type of insurance coverage do you have?
___ Medicare
___ Medicaid
___ private insurance
___ military health insurance
___ no insurance coverage

Please place an X in the box that best describes your answer to the question.

In general…

	Excellent	Very Good	Good	Fair	Poor
would you say your quality of life is …					
how would you rate your physical health?					
how would you rate your mental health, including your mood and ability to think?					
how would you rate your satisfaction with your social activities and relationships?					

***** Please continue the survey on the back of this page. *****

What do you think are the chances that your cancer will come back or get worse within the next 10 years? Would you say…

___ very low
___ fairly low
___ moderate
___ fairly high
___ very high

How often do you worry that your cancer may come back or get worse? Would you say…

___ never
___ rarely
___ sometimes
___ often
___ all the time

Please list your phone number and email so that we can contact your for the short 4 question surveys at the 1-week and 2-week time points. This information will be securely shredded and discarded after completion of the survey.

Phone number: __(_____)_____-_____

Email: _____

***** Please continue the survey on the next page. *****

Physical Activity Questionnaire

The questions below are about the sports and recreational physical activities you participated in during the **past 6 months.** Feel free to leave blank irrelevant activities, but otherwise, please fill in each row to completion.

	1. Activity Name	2. Average Times/week	3. Average Min/Time	4. # Months
01	**Walking** for exercise (outdoor or treadmill)			
02	**Jogging/running**			
03	**Hiking**			
04	**Bicycling** (including stationary)			
05	**Aerobics**			
06	**Stairmaster**			
07	**Elliptical**			
08	**Nordic Track**			
09	**Rowing machine**			
10	**Weight lifting** (free or Nautilus)			
11	**Swimming laps**			
12	**Water aerobics**			
13	**Yoga**			
14	**Pilates**			
15	**Tennis**			
16	**Racquetball/Squash**			
17	**Golf without cart**			
18	**Downhill Skiing**			
19	**Cross-country skiing**			
208	**Fast dancing**			
21	**Other**			
220	**Other**			

***** Please hand this survey to your surgeon, who will complete the questions on the following page *****

What type of surgery did this patient receive?
___ lumpectomy/partial mastectomy
___ conventional mastectomy with no reconstruction
___ skin-sparing mastectomy with reconstruction

How long ago was the surgery?
_____ days
_____ weeks
_____ months
_____ years

Did this patient receive conventional chemotherapy?
___ yes
___ no

Did this patient receive radiation therapy?
___ yes
___ no

Was this patient treated with Herceptin?
___ yes
___ no

Was this patient treated with tamoxifen?
___ yes
___ no

Was this patient treated with an aromatase inhibitor?
___ yes
___ no

Please place completed study paperwork in the designated envelope in the fishbowl

References

1. Stromgren AS, Niemann CU, Tange UB, et al: Quality of life and symptoms in patients with malignant diseases admitted to a comprehensive cancer centre. Support Care Cancer 22:1843-9, 2014
2. So WK, Chan RJ, Chan DN, et al: Quality-of-life among head and neck cancer survivors at one year after treatment--a systematic review. Eur J Cancer 48:2391-408, 2012
3. Howard-Anderson J, Ganz PA, Bower JE, et al: Quality of life, fertility concerns, and behavioral health outcomes in younger breast cancer survivors: a systematic review. J Natl Cancer Inst 104:386-405, 2012
4. Flanagan JC: Measurement of quality of life: current state of the art. Arch Phys Med Rehabil 63:56-9, 1982
5. Flanagan JC: A research approach to improving our quality of life. American Psychologist 33:138, 1978
6. Patterson WB: The quality of survival in response to treatment. JAMA 233:280-1, 1975
7. Jacobsen PB, Jim HS: Consideration of quality of life in cancer survivorship research. Cancer Epidemiol Biomarkers Prev 20:2035-41, 2011
8. Coons SJ, Rao S, Keininger DL, et al: A Comparative Review of Generic Quality-of-Life Instruments. PharmacoEconomics 17:13-35, 2000
9. Mariotto AB, Yabroff KR, Shao Y, et al: Projections of the cost of cancer care in the United States: 2010-2020. J Natl Cancer Inst 103:117-28, 2011
10. Caspersen CJ, Powell KE, Christenson GM: Physical activity, exercise, and physical fitness: definitions and distinctions for health-related research. Public Health Rep 100:126-31, 1985
11. Saxton J, Daley A: Exercise Terminology, in Saxton J, Daley A (eds): Exercise and Cancer Survivorship: Impact on Health Outcomes and Quality of Life. New York, NY, Springer, 2010
12. Winter EM, Fowler N: Exercise defined and quantified according to the Systeme International d'Unites. J Sports Sci 27:447-60, 2009
13. Warburton DE, Nicol CW, Bredin SS: Health benefits of physical activity: the evidence. CMAJ 174:801-9, 2006
14. Go4Life, National Institute on Aging at NIH
15. Shephard RJ: Limits to the measurement of habitual physical activity by questionnaires. Br J Sports Med 37:197-206; discussion 206, 2003
16. Courneya KS, Friedenreich CM: Physical Activity, Exercise, and Health-Related Fitness, in Courneya KS, Friedenreich CM (eds): Physical Activity and Cancer. Recent Results in Cancer Research. Berlin-Heidelberg, Springer, 2010
17. Division of Nutrition PAaO, National Center for Chronic Disease Prevention and Health Promotion: Measuring Physical Activity, Physical Activity for Everyone, Centers for Disease Control and Prevention, 2011
18. Division of Nutrition PAaO, National Center for Chronic Disease Prevention and Health Promotion: How much physical activity do adults need?, Centers for Disease Control and Prevention

19. Thomson W, Gordon N, Prescatello L: ACSM's Guidelines for Exercise Testing and Prescription Eighth Edition. Baltimore, Maryland, Lippincott Williams and Wilkins, 2010 pp. 54
20. Gibbons RJ, Balady GJ, Bricker JT, et al: ACC/AHA 2002 guideline update for exercise testing: summary article: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Update the 1997 Exercise Testing Guidelines). Circulation 106:1883-92, 2002
21. Schmitz KH, Irwin M, Speck RM: Effects of Physical Activity on Persistent Effects of Cancer Treatment, in McTiernan A (ed): Physical Activity, Dietary Calorie Restriction, and Cancer. Energy Balance and Cancer. New York, NY, Springer, 2011
22. MF L: Physical activity and genitourinary cancer prevention, in Courneya KS, Friedenreich CM (eds): Physical activity and cancer: Recent results in cancer research. Berlin Heidelberg, Springer, 2011
23. SY P, H M: Physical activity and hematologic cancer prevention, in Courneya KS, Friedenreich CM (eds): Physical activity and cancer: Recent results in cancer research. Berlin Heidelberg, Springer, 2011
24. Ligibel JA, Campbell N, Partridge A, et al: Impact of a mixed strength and endurance exercise intervention on insulin levels in breast cancer survivors. J Clin Oncol 26:907-12, 2008
25. Lund Haheim L, Wisloff TF, Holme I, et al: Metabolic syndrome predicts prostate cancer in a cohort of middle-aged Norwegian men followed for 27 years. Am J Epidemiol 164:769-74, 2006
26. Rundle A: Summary of many of the proposed mechanisms linking physical acitivity to lower cancer risk. Physical Activity, Dietary Calorie Restriction, and Cancer, Springer, 2011
27. Mishra SI, Scherer RW, Geigle PM, et al: Exercise interventions on health-related quality of life for cancer survivors. Cochrane Database Syst Rev 8:CD007566, 2012
28. Solberg Nes L, Liu H, Patten CA, et al: Physical activity level and quality of life in long term lung cancer survivors. Lung Cancer 77:611-6, 2012
29. Speck RM, Courneya KS, Masse LC, et al: An update of controlled physical activity trials in cancer survivors: a systematic review and meta-analysis. J Cancer Surviv 4:87-100, 2010
30. Hanmer J, Lawrence WF, Anderson JP, et al: Report of nationally representative values for the noninstitutionalized US adult population for 7 health-related quality-of-life scores. Med Decis Making 26:391-400, 2006
31. Salomon JA, Nordhagen S, Oza S, et al: Are Americans feeling less healthy? The puzzle of trends in self-rated health. Am J Epidemiol 170:343-51, 2009
32. Binder DA: On the Variances of Asymptotically Normal Estimators from Complex Surveys. International Statistical Review 51:279-292, 1983
33. McNeely ML, Parliament M, Courneya KS, et al: A pilot study of a randomized controlled trial to evaluate the effects of progressive resistance exercise training on shoulder dysfunction caused by spinal accessory

neurapraxia/neurectomy in head and neck cancer survivors. Head and Neck-Journal for the Sciences and Specialties of the Head and Neck 26:518-530, 2004

34. McNeely ML, Parliament MB, Seikaly H, et al: Effect of exercise on upper extremity pain and dysfunction in head and neck cancer survivors - A randomized controlled trial. Cancer 113:214-222, 2008

35. Duffy SA, Ronis DL, McLean S, et al: Pretreatment Health Behaviors Predict Survival Among Patients With Head and Neck Squamous Cell Carcinoma. Journal of Clinical Oncology 27:1969-1975, 2009

36. Rogers LQ, Courneya KS, Robbins KT, et al: Physical activity and quality of life in head and neck cancer survivors. Supportive Care in Cancer 14:1012-1019, 2006

37. Rogers LQ, Anton PM, Fogleman A, et al: Pilot, randomized trial of resistance exercise during radiation therapy for head and neck cancer. Head and Neck-Journal for the Sciences and Specialties of the Head and Neck 35:1178-1188, 2013

38. Eades M, Murphy J, Carney S, et al: Effect of an interdisciplinary rehabilitation program on quality of life in patients with head and neck cancer: review of clinical experience. Head Neck 35:343-9, 2013

39. Lonbro S, Dalgas U, Primdahl H, et al: Progressive resistance training rebuilds lean body mass in head and neck cancer patients after radiotherapy - Results from the randomized DAHANCA 25B trial. Radiotherapy and Oncology 108:314-319, 2013

40. Zhou J, Alexander N, Schipper M, et al: The Effect of Resistance Exercise Training on Health-Related Quality of Life of Head-and-Neck Cancer Patients Undergoing Definitive Chemoradiation: Results of a Pilot Study. International Journal of Radiation Oncology Biology Physics 87:S569-S570, 2013

41. Samuel SR, Maiya GA, Babu AS, et al: Effect of exercise training on functional capacity & quality of life in head & neck cancer patients receiving chemoradiotherapy. Indian J Med Res 137:515-20, 2013

42. Capozzi LC, Boldt KR, Lau H, et al: A clinic-supported group exercise program for head and neck cancer survivors: managing cancer and treatment side effects to improve quality of life. Support Care Cancer, 2014

43. Lonbro S, Dalgas U, Primdahl H, et al: Lean body mass and muscle function in head and neck cancer patients and healthy individuals--results from the DAHANCA 25 study. Acta Oncol 52:1543-51, 2013

44. Lonbro S, Dalgas U, Primdahl H, et al: Feasibility and efficacy of progressive resistance training and dietary supplements in radiotherapy treated head and neck cancer patients - the DAHANCA 25A study. Acta Oncologica 52:310-318, 2013

45. Fong SSM, Ng SSM, Luk WS, et al: Effects of a 6-month Tai Chi Qigong program on arterial hemodynamics and functional aerobic capacity in survivors of nasopharyngeal cancer. Journal of Cancer Survivorship 8:618-626, 2014

46. Samuel SR, Arun Maiya G, Babu AS, et al: Effect of exercise training on functional capacity & quality of life in head & neck cancer patients receiving chemoradiotherapy. Indian Journal of Medical Research 137:515-520, 2013

47. Aghili M, Farhan F, Rade M: A pilot study of the effects of programmed aerobic exercise on the severity of fatigue in cancer patients during external radiotherapy. Eur J Oncol Nurs 11:179-82, 2007
48. Chen YJ, Lai YH, Lee YH, et al: Relationship of fatigue, exercise intensity, depression, physical status and fatigue related factors in head and neck cancer survivors in Taiwan. Psycho-Oncology 22:324-325, 2013
49. Aghili M, Farhan F, Rade M: A pilot study of the effects of programmed aerobic exercise on the severity of fatigue in cancer patients during external radiotherapy. European Journal of Oncology Nursing 11:179-182, 2007
50. Rogers LQ, Courneya KS, Robbins KT, et al: Factors associated with fatigue, sleep, and cognitive function among patients with head and neck cancer. Head and Neck-Journal for the Sciences and Specialties of the Head and Neck 30:1310-1317, 2008
51. Shuman AG, Terrell JE, Light E, et al: Predictors of Pain Among Patients With Head and Neck Cancer. Archives of Otolaryngology-Head & Neck Surgery 138:1147-1154, 2012
52. CM S, S CK: Physical activity and gastrointestinal survivorship, in Courneya KS, Friedenreich CM (eds): Physical activity and cancer: Recent results in cancer research. Berlin Heidelberg, Springer, 2011
53. K S: Physical activity and breast cancer survivorship, in Courneya KS, Friedenreich CM (eds): Physical activity and cancer: Recent results in cancer research. Berlin Heidelberg, Springer, 2011
54. Tewari A, Irwin M, Chagpar A: Abstract 5039: Physical activity is associated with improved quality of life in cancer survivors: A population-based analysis. Cancer Research 74:5039, 2014
55. Santa Mina D, Guglietti CL, Alibhai SM, et al: The effect of meeting physical activity guidelines for cancer survivors on quality of life following radical prostatectomy for prostate cancer. J Cancer Surviv 8:190-8, 2014
56. Kenfield SA, Stampfer MJ, Giovannucci E, et al: Physical activity and survival after prostate cancer diagnosis in the health professionals follow-up study. J Clin Oncol 29:726-32, 2011
57. Chaukar DA, Walvekar RR, Das AK, et al: Quality of life in head and neck cancer survivors: a cross-sectional survey. Am J Otolaryngol 30:176-80, 2009
58. Jacobsen PB, Thors CL: Fatigue in the radiation therapy patient: current management and investigations. Semin Radiat Oncol 13:372-80, 2003
59. Sawada NO, de Paula JM, Sonobe HM, et al: Depression, fatigue, and health-related quality of life in head and neck cancer patients: a prospective pilot study. Support Care Cancer 20:2705-11, 2012
60. Mirowsky J, Ross C: Education, Social Status, and Health. Hawthorne, NY, Aldine De Gruyter, 2003
61. 2008 Physical Activity Guidelines for Americans, in Services DoHaH (ed). Washington D.C., ODPHP, 2008
62. Loprinzi PD, Lee H, Cardinal BJ: Objectively measured physical activity among US cancer survivors: considerations by weight status. J Cancer Surviv 7:493-9, 2013

63. Nayak P, Holmes HM, Nguyen HT, et al: Self-reported physical activity among middle-aged cancer survivors in the United States: Behavioral Risk Factor Surveillance System Survey, 2009. Prev Chronic Dis 11:E156, 2014

64. Phillips SM, McAuley E: Physical activity and quality of life in breast cancer survivors: the role of self-efficacy and health status. Psychooncology 23:27-34, 2014

65. Segal RJ, Reid RD, Courneya KS, et al: Randomized controlled trial of resistance or aerobic exercise in men receiving radiation therapy for prostate cancer. J Clin Oncol 27:344-51, 2009

66. Louwman WJ, van Lenthe FJ, Coebergh JW, et al: Behaviour partly explains educational differences in cancer incidence in the south-eastern Netherlands: the longitudinal GLOBE study. Eur J Cancer Prev 13:119-25, 2004

67. Inoue-Choi M, Lazovich D, Prizment AE, et al: Adherence to the World Cancer Research Fund/American Institute for Cancer Research recommendations for cancer prevention is associated with better health-related quality of life among elderly female cancer survivors. J Clin Oncol 31:1758-66, 2013

68. Pampel FC, Krueger PM, Denney JT: Socioeconomic Disparities in Health Behaviors. Annu Rev Sociol 36:349-370, 2010

69. Bourdieu P: Distinction: A Social Critique of the Judgment of Taste. Cambridge, MA, Harvard University Press, 1984

70. C S: Adult participation in sports as cultural capital: a test of Bourdieu's theory of the field of sports. Int Rev Sociol Sport 40:411-432, 2005

71. Jones SB, Thomas GA, Hesselsweet SD, et al: Effect of exercise on markers of inflammation in breast cancer survivors: the Yale exercise and survivorship study. Cancer Prev Res (Phila) 6:109-18, 2013

72. Mols F, Vingerhoets AJ, Coebergh JW, et al: Quality of life among long-term breast cancer survivors: a systematic review. Eur J Cancer 41:2613-9, 2005

73. Ohira T, Schmitz KH, Ahmed RL, et al: Effects of weight training on quality of life in recent breast cancer survivors: the Weight Training for Breast Cancer Survivors (WTBS) study. Cancer 106:2076-83, 2006

74. Cheema BS, Gaul CA: Full-body exercise training improves fitness and quality of life in survivors of breast cancer. J Strength Cond Res 20:14-21, 2006

75. De Backer IC, Van Breda E, Vreugdenhil A, et al: High-intensity strength training improves quality of life in cancer survivors. Acta Oncol 46:1143-51, 2007

76. Keogh JW, MacLeod RD: Body composition, physical fitness, functional performance, quality of life, and fatigue benefits of exercise for prostate cancer patients: a systematic review. J Pain Symptom Manage 43:96-110, 2012