ASSOCIATIONS OF PHYSICAL ACTIVITY AND SEDENTARY BEHAVIOR WITH LIFE EXPECTANCY FREE OF CARDIOVASCULAR DISEASE AND CANCER

Carmen Carol Cuthbertson

A dissertation submitted to the faculty at the University of North Carolina at Chapel Hill in partial fulfillment of the requirements for the degree of Doctor of Philosophy in the Department of Epidemiology in the Gillings School of Global Public Health.

Chapel Hill
2019

Approved by:

Kelly R. Evenson

Gerardo Heiss

Anna Kucharska-Newton

Hazel B. Nichols

Xianming Tan

ABSTRACT

Carmen Carol Cuthbertson: Associations of physical activity and sedentary behavior with life expectancy free of cardiovascular disease and cancer
(Under the direction of Kelly R. Evenson)

Engagement in high levels of physical activity have been linked to a lower risk of cardiovascular disease (CVD), cancer, and all-cause mortality. Conversely, greater amounts of sedentary behavior have been associated with an increased risk of these outcomes. Participation in more physical activity compared to less has also been associated with longer disease-free life expectancy from composite measures of chronic disease. However, research in this area has not included cancer outcomes or examined sedentary behavior.

This dissertation quantified the associations of physical activity and sedentary behavior with life expectancy free of three types of nonfatal CVD (coronary heart disease, stroke, and heart failure) and four types of cancer (colorectal, lung, prostate, and postmenopausal breast cancer). Analysis was conducted on data from the Atherosclerosis Risk in Communities Study (1987 – 2016). We included 13,534 participants in the CVD analyses and 14,508 participants in the cancer analyses. Life expectancies were estimated separate for men and women.

Across all diseases, engagement in LTPA was associated in an inverse dose-response fashion with life expectancy free of each disease. Engaging in LTPA less than the median compared to no LTPA was associated with 0.8 – 1.3 year greater CVD- and cancer-free life expectancy. Engaging in LTPA greater than or equal to the median compared to no LTPA was

associated with a longer disease-free life expectancy for coronary heart disease (men-1.5 years, women-1.6 years), stroke (men-1.8 years, women-1.8 years), heart failure (men-1.6 years, women-1.7 years), colorectal cancer (men-2.2 years, women-2.3 years), lung cancer (men-2.1 years, women-2.1 years), prostate cancer (1.5 years), and postmenopausal breast cancer (2.4 years). Viewing TV seldom/never compared to often/very often viewing was associated with longer CVD- and cancer-free life expectancy of 0.8 – 1.2 years for men and women and all diseases except prostate cancer.

These findings suggest that engaging in more LTPA and viewing less TV may contribute to living more years free of many types of CVD and cancer.

ACKNOWLEDGEMENTS

I would like to thank my advisor, Dr. Kelly Evenson, for her support and guidance throughout my graduate school career. I have greatly appreciated her mentorship and advice over the past six years. I want to thank my committee members for their support and interest in my dissertation research. In particular, I would like to thank Dr. Xianming Tan for his guidance and help in learning multistate models and life expectancies; I am appreciative of Dr. Anna Kucharska-Newton, for her support and mentorship throughout my time as a PhD student; I would like to thank Dr. Gerardo Heiss for his thoughtful questions and feedback; and I am grateful to Dr. Hazel Nichols for her guidance and support, especially in the area of cancer epidemiology. Outside of my committee, I would like to thank Dr. Chirayath M. Suchindran for his assistance in explaining multistate models and life expectancies.

I thank my partner, Dean Farrell, for his continued support as I made a substantial career and life change to go back to graduate school. I also want to thank my family and Dean's family for being supportive of my career change and for their interest in my dissertation research. I am grateful to my friends for their support. I especially want to acknowledge the friends I made during graduate school -- Shelly-Ann Love, Ann Von Holle, and Jennifer Yourkavitch. We all made mid-career changes to go back to school and shared valuable experiences together.

Most of my dissertation research was funded by a National Heart, Lung, and Blood Institute National Research Service Award (NRSA:T32-HL007055-41). I thank the staff and participants of the ARIC study for their important contributions. The ARIC study was supported

by federal funds from the National Heart, Lung, and Blood Institute, National Institutes of Health, Department of Health and Human Services, under Contract nos. (HHSN268201700001I, HHSN268201700002I, HHSN268201700003I, HHSN268201700005I, HHSN268201700004I). Studies on cancer in ARIC are also supported by the National Cancer Institute (U01 CA164975). Cancer incidence data have been provided by the Maryland Cancer Registry, Center for Cancer Surveillance and Control, Department of Mental Health and Hygiene, 201 W. Preston Street, Room 400, Baltimore, MD 21201. We acknowledge the State of Maryland, the Maryland Cigarette Restitution Fund, and the National Program of Cancer Registries (NPCR) of the Centers for Disease Control and Prevention (CDC) for the funds that helped support the availability of the cancer registry data.

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LIST OF ABBREVIATIONS

AICR	American Institute for Cancer Research
ARIC	Atherosclerosis Risk in Communities
BMI	Body mass index
CDC	Centers for Disease Control and Prevention
CHD	Coronary heart disease
CI	Confidence interval
CUP	Continuous Update Report
CVD	Cardiovascular disease
DALYs	Disability adjusted life years
ELECT	Estimating Life Expectancies in Continuous Time
EU	European Union
GBD	Global Burden of Disease
HALE	Healthy adjusted life expectancy
HDL-C	High-density lipoprotein cholesterol
HF	Heart failure
HR	Hazard ratio
IGF-1	Insulin-like growth factor 1
IL	Interleukin
LE	Life expectancy
LPL	Lipoprotein lipase
LTPA	Leisure-time moderate-to-vigorous physical activity
MET	Metabolic equivalent of task

MHT	Menopausal hormone therapy
MI	Myocardial infarction
MICE	Multiple imputation by chained equations
NCI	National Cancer Institute
NHANES	National Health and Nutrition Examination Survey
PA	Physical activity
PAG	Physical activity guidelines
PSA	Prostate specific antigen
RR	Risk ratio
TNF	Tumor necrosis factor
TV	Television viewing
UI	Uncertainty Intervals
US	United States
YLD	Years lived with disability
YLL	Years of life lost
WCRF	World Cancer Research Fund

CHAPTER 1: INTRODUCTION

Chronic diseases are the leading cause of death, premature mortality, and years lived with disability in the United States (US). [1, 2] Although chronic disease mortality rates have declined and life expectancy has increased, many adults are living longer in poor health.[2] In 2010, the average US life expectancy at birth was 78.2 years but adults could expect to live at least 10 years with illness and disability.[2] The major contributors to the chronic disease burden are cardiovascular disease (CVD) and cancer. [3] The major CVDs are coronary heart disease (CHD), stroke, and heart failure (HF) [4] and the leading cancers are breast, prostate, lung, and colorectal cancer. [5]

Two modifiable behaviors linked to these chronic diseases are physical activity and sedentary behavior. Consistent epidemiological evidence suggests physical activity reduces the risk of CHD, stroke, HF, postmenopausal breast cancer, colorectal cancer, lung cancer, and prostate cancer. [6, 7] Sedentary behavior, conversely, is linked to increasing the risk of these diseases. [8, 9] Three studies have used health expectancy outcomes, defined as a class of metrics that combine morbidity and mortality information, to estimate life expectancy free of CVD by level of physical activity. Findings from these studies suggested that participation in greater amounts of physical activity compared to lower levels was associated with a longer CVD-free life expectancy.[10-12] Research in this area has been limited to use of physical activity measurements that are challenging to generalize to other populations and to studies without

cancer outcomes. In addition, no studies using health expectancy outcomes have included sedentary behavior.

This dissertation examined how physical activity and sedentary behavior were associated with CVD and cancer life expectancy outcomes. The first aim evaluated the association of leisure-time physical activity with life expectancy free of three CVDs (CHD, stroke, HF) and four cancers (postmenopausal breast cancer, colorectal cancer, lung cancer, prostate cancer). The second aim evaluated the association of sedentary behavior with the same outcomes. Our findings suggested that engaging in more physical activity compared to no physical activity and less TV viewing compared to more viewing were associated with living more years free of seven leading chronic diseases. Identifying interventions that extend the number of healthy years is a priority for improving and maintaining the health of older adults, as this population is expected to increase, [13] and the current chronic disease burden suggests many years may be spent managing illness and disability.

CHAPTER 2: STATEMENT OF SPECIFIC AIMS

Aim 1: To evaluate the association of physical activity with disease-free life expectancy at age 50.

Hypothesis 1.1: There is a positive dose response relationship between leisure-time moderate-to-vigorous physical activity (LTPA) with disease-free life expectancy for three CVDs (CHD, stroke, HF) and four cancers (colorectal, lung, prostate, breast).

Aim 2: To evaluate the association of sedentary behavior with disease-free life expectancy at age 50.

Hypothesis 2.1: There is an inverse dose response relationship between TV viewing with disease-free life expectancy for three CVDs (CHD, stroke, HF) and four cancers (colorectal, lung, prostate, breast).

CHAPTER 3: BACKGROUND AND REVIEW OF THE LITERATURE

3.1 Life expectancy and chronic disease

3.1.1 Population aging and life expectancy

Populations are aging worldwide and are predicted to continue to increase in average age. In 2015, 8.5% (617.1 million) of the worldwide population was 65 or older and this proportion is predicted to be 12% (998.7 million) by 2030 and 16.7% (1,565.8 million) by 2050.[13] Part of the increase in the older adult population is because life expectancy has increased over the past 100 years.[13]

In the United States (US) in 2014, life expectancy at birth was 78.8 years, at age 50 was 31.6 years, and at age 65 was 19.3 years (Table 1).[14] In examining differences by race and gender, white females at any age have the longest life expectancy, followed by African American females and white males. The lowest life expectancy across all ages is for African American males. As displayed in Figure 1, the magnitude of life expectancy differences by race and gender has decreased over time, but disparities are still observed.

Figure 1. Life expectancy at birth by gender and race in the US.

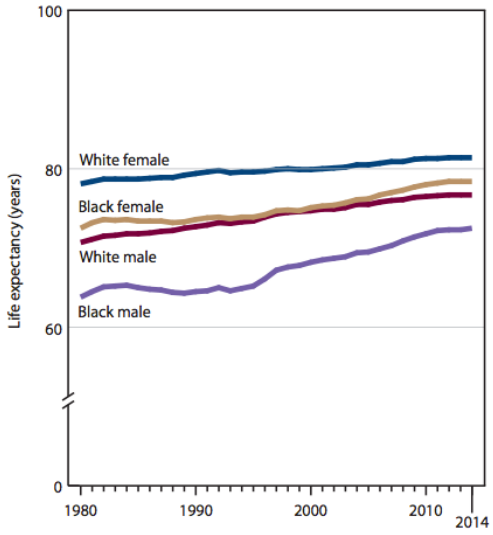


Figure 1 from [15].

Table 1. Life expectancy at birth, age 50, and age 65 by race and gender in 2014 in the US.

	At birth	Age 50	Age 65
Overall	78.8	31.6	19.3
White male	76.7	29.9	18.0
Black male	72.5	27.1	16.3
White female	81.4	33.4	20.5
Black female	78.4	31.5	19.6

Life expectancy estimates from [14].

3.1.2 Burden of chronic disease

Over the past 100 years mortality due to infectious diseases has declined and mortality due to chronic diseases has increased. In the early 1900's, the top causes of death were pneumonia or influenza, tuberculosis, and gastrointestinal infections.[16] By 2014, the top causes of death were heart disease and cancer, accounting for 45.9% of all deaths across race and gender groups.[3]

CVD and cancer are not only the leading causes of death, but they also cause a large burden of morbidity. The Global Burden of Disease (GBD) project estimates metrics that inform on morbidity and mortality due to individual diseases. Some of the metrics the GBD uses include years of life lost due to premature mortality (YLL), years lived with disability (YLD), and disability-adjusted life years (DALYs). In 2016 in the US, the top three diseases contributing to YLL were ischemic heart disease, lung cancer, and chronic obstructive pulmonary disease.[17] Other leading contributors to YLL were colorectal cancer (ranked 5th), stroke (ranked 10th),

breast cancer (ranked11th); prostate cancer was not among the leading YLL causes. The only CVD or cancer that was a leading cause of YLD was stroke (ranked 15th). DALYs represent a health gap between current health status and ideal health. In terms of DALYs, the leading causes were ischemic heart disease, lung cancer, and chronic obstructive pulmonary disease. Stroke was ranked 12th, colorectal cancer 17th, breast cancer 20st, and prostate cancer was not in the top 25 leading causes of DALYs.[17] In summary, many types of CVD and cancer contribute to premature mortality and loss of healthy life years.

3.1.3 Health expectancy measures

The increase in life expectancy, accompanied by high rates of chronic disease, suggest the years of life gained may not be spent in good health. Therefore, metrics that inform on the number of years spent in good and poor health are valuable for monitoring population health. Health expectancy measures are a class of metrics that combine morbidity and mortality information to reflect the average number of years a person can expect to live in full health. [18-21] These measures combine quantity and quality of life and can be more informative than life expectancy alone. These measures can complement other population health measures (i.e., incidence, prevalence) that do not inform on how long a person lives with disease or disability. This type of information can illustrate if years of life spent unhealthy are expanding or decreasing with the increase in life expectancy. Governments and policymakers can use this information to set realistic retirement ages, to plan for pensions, and predict health care and long term care needs and costs.[22] Health expectancy measures include active life expectancy, disability-free life expectancy, healthy life expectancy, disease-specific free life expectancy, and healthy adjusted life expectancy (HALE).

Health expectancy measures differ in how health is defined (Table 2). [22] For example, active life expectancy uses dependency in activities of daily living to define health. Similarly, disability-free life expectancy is constructed using functional limitations. Healthy life expectancy is often constructed using self-rated health. The GBD metric of HALE is based on over 220 distinct states of health and disability associated with those states.[18] The health expectancy outcome used less often is disease specific free life expectancy.

Of the studies that examined disease specific free life expectancy, outcomes have included CVD,[10-12, 23, 24] diabetes,[25] and chronic disease (combination of many diseases).[26-29] A recent systematic review on health expectancy measures among older adults identified 90 studies; 76 of these studies measured health expectancy with either dependency in activities of daily living or difficulty in functional limitations and 14 studies used self-rated health.[22] However, studies that examined disease specific free life expectancy (i.e., CVD, diabetes, chronic diseases) were not included in this review.

Table 2. Description of different health expectancy measures.

Term	Definition
Active life expectancy	Number of years a person is expected to live without restrictions in activities of daily living
Disability-free life expectancy	Number of years a person is expected to live free of disability often measured by functional limitations
Healthy life expectancy	Number of years a person is expected to live in full health, often measured with self-rated health
Disease specific free life expectancy	Number of years a person is expected to live without specific diseases

Calculations of health expectancy outcomes can inform on average years of life spent in good health and lost to poor health. By examining the years spent in poor health over time, observations can be made regarding whether years spent in poor health have increased,

decreased, or remained the same. For example, the GBD estimated HALE in 1990 and 2010 in the US. During the time period, both life expectancy and HALE at birth increased. Life expectancy increased from 75.2 years (95% Uncertainty Intervals (UI) 75.2, 75.2) to 78.2 years (95% UI 78.2, 78.3) and HALE increased from 65.8 years (95% UI 64.0, 67.4) to 68.1 years (95% UI 66.3, 69.8). However, the gap between HALE and life expectancy also increased so that the gap in 1990 was 9.4 years and in 2010 was 10.1 years.[2] This finding suggests that although people are living longer, the years spent in poor health have also increased.

3.1.4 Summary

As population aging continues, interest has grown in understanding how to delay the onset of chronic diseases to increase the years spent in good health. Health expectancy outcomes can aid in research in this area by highlighting years spent in good health. Given that CVD and cancer contribute to a large burden of morbidity and mortality, targeting the prevention of these diseases could extend the number of years lived in health free of these diseases.

3.2 Overview of CVD and cancer

3.2.1 Overview of cardiovascular disease

In 2014, an estimated 92.1 million (36.6%) people in the US had been diagnosed with CVD.[30] The leading causes of death from CVD are CHD (44%) and stroke (17%).[30] As referenced by acute care hospitalizations, CHD is the most frequent, followed by stroke and HF.[31] Likelihood of developing CVD increases with age and with presence of multiple risk factors.[30] Many CVDs share the same risk factors including high blood pressure, obesity, adverse blood lipid profiles, diabetes, smoking, low levels of physical activity, excess alcohol consumption, and family history of CVD.[31]

Cardiovascular diseases include disorders of the heart and the arteries supplying blood flow to the heart, brain, and peripheral tissues.[31] A common underlying factor in the development of many CVDs is atherosclerosis. Atherosclerosis is a process that alters the walls of the medium and large arteries that supply the heart, brain, lower extremities, and the aorta.[31] The early stages of atherosclerosis are characterized by raised lesions typically at sites of fatty streaks. The lesions can develop into fibrous plaques and eventually become stenotic or complicated lesions that restrict blood flow.[31] In industrialized societies atherosclerotic lesions begin in childhood but the development of a CVD manifestation associated with atherosclerosis usually occurs later in life.[31]

CHD is syndrome that includes angina pectoris, acute myocardial infarction (MI), complications following acute MI, and chronic ischemic heart disease.[31] About 16.5 million Americans (6.3%) have CHD.[30] Both CHD death rates and incidence rates have declined over the past decade.[30]

Stroke refers to sudden neurologic deficits as a consequence of impaired blood flow in the brain.[31] In the US, 2.7 million Americans have had a stroke (2.7%).[30] Close to 800,000 people are estimated to have a new or recurrent stroke each year - 77% of these are first attacks and 23% are recurrent attacks. Most strokes are ischemic (87%), 10% are intracerebral hemorrhage, and 3% are subarachnoid hemorrhage.[30] Multiple studies suggest stroke incidence and mortality has declined over time for both men and women and all race and age groups.

HF is a syndrome that results from impairment of the pumping function of the left ventricle of the heart or an increase in stiffness of the ventricles. About 6.5 million Americans have HF (National Health and Nutrition Examination Survey (NHANES) 2011-2014 data cycle).[30] Incidence rates are highest for African Americans compared to whites.[30] Case fatality is

high for people diagnosed with heart failure. About 50% of people diagnosed with heart failure will die within five years.[30]

3.2.2 Overview of cancer

In the US in 2018, over 15.5 million people had ever been diagnosed with cancer and about 1.69 million new cancer cases are predicted to be diagnosed in 2018.[32]

The leading cancers for men are prostate (19%), lung and bronchus (14%), and colon and rectum (9%). The leading cancers for women are breast (30%), lung and bronchus (12%), and colon and rectum (8%).[5] Most cancer is diagnosed in older adults, as about 87% occurs in people 50 years and older.[5] The cancer death rate increased over the 20th century due to smoking and peaked in 1991 at 215 deaths per 100,000 persons. This death rate has declined to 161 deaths per 100,000 persons in 2014 due to declines in death rates from lung, colorectal, breast, and prostate cancer.[5]

Cancer is a group of related diseases that results from the uncontrolled growth and spread of abnormal cells.[5] Normal cells can become damaged by factors that alter cell DNA that can arise from genetic factors and external agents such naturally occurring exposures (i.e. ultraviolet radiation), lifestyle factors (i.e. diet), workplace and household exposures, medical treatments (i.e. hormone drugs), and pollution.[33] The cancerous cells can progress to pre-cancerous lesions and to a malignant tumor. Metastasis occurs if cells break away from a tumor and move to other areas of the body to start a new site and continue growing.[34]

Colorectal cancer is the third leading incident cancer and accounts for 9% and 8% of detected cancers among men and women, respectively.[5] Over 1.3 million people in the US have been diagnosed with colorectal cancer.[35] Colorectal cancer incidence and death rates have declined for several decades due improvements in cancer screening and treatment.[5] Risk factors for colorectal cancer include obesity, low levels of physical activity, smoking, high consumption

of red or processed meat, low calcium intake, moderate to heavy alcohol intake, low intake fruits, vegetables and whole grain fiber, family history of colorectal cancer, and type 2 diabetes.[5]

Lung cancer is the second leading cancer for men and women, accounting for 14% and 13% of incident cancers, respectively.[5] Over 541,000 people in the US have been diagnosed with lung cancer.[35] The incidence rates have declined since 1980's for men and 2000's for women, due to reductions in smoking. Similarly, lung cancer death rates have also declined.[5] Risk factors for lung cancer include smoking, exposure to environmental factors (radon gas, asbestos), certain metals (chromium, arsenic, cadmium), radiation, air pollution, and diesel exhaust.[5]

Among women, breast cancer is the most frequently detected cancer accounting for about 30% of incident cancers.[5] Over 3.4 million people in the US have been diagnosed with breast cancer.[35] Invasive breast cancer incidence rates for white women have remained stable from 2004 to 2013 and rates for African American women have increased 0.5% to an incidence rate very similar to that of white women.[5] The mortality rate for breast cancer has declined by 38% from 1989 to 2014 due to better detection and treatment.[5] Risk factors for breast cancer include overweight/obesity, postmenopausal hormone use, low levels of physical activity, alcohol, family history of breast or ovarian cancer, inherited mutations (such as in *BRCA1*, *BRCA2*), high breast tissue density, high dose radiation to the chest when young, and reproductive history factors (long menstrual history, never having children, and having first child after age 30). [5]

Among men, prostate cancer is the leading cancer accounting for 19% of deaths due to cancer.[5] The prevalence of prostate cancer in 2015 was 2.8 million in the US.[35] The incidence rate for prostate cancer increased in late 1980's because of higher uptake of prostate screening (with prostate-specific antigen (PSA) test). The rate declined in the year 2000 and has continued to decline mostly due to guideline changes in 2008 to stop routine PSA screening.[5] The age-

adjusted incidence rate is higher for African American men (203.5 cases per 100,000 population) than white men (121.9 cases per 100,000 population).[36] Well-established risk factors for prostate cancer include age, African ancestry, family history of prostate cancer, and inherited conditions (Lynch syndrome and *BRCA1* and *BRCA2* mutations).[5]

3.2.3 Summary

Much progress has been made over the decades in reducing incidence rates and improving survival for the leading CVDs and cancers. Common to these diseases are many of the same risk factors. For example, low levels of physical activity are a risk factor for each disease described. Interventions to improve habitual physical activity may be one strategy to increase years spent in health by preventing and/or delaying the onset of these leading diseases.

3.3 Physical activity and sedentary behavior

3.3.1 Physical activity

Physical activity is defined as "any bodily movement produced by skeletal muscles that results in energy expenditure" and includes activity that occurs while working, commuting, performing household chores, and participating in any planned exercise or sport.[37] The most commonly used method for gathering physical activity data in epidemiological studies is self-report questionnaires[37] and leisure-time (e.g., discretionary) activity is the domain most often asked about.[4]

Physical activity is often measured by collecting information on the frequency (how often activity is done), duration (how long activity lasted), and intensity (the level of effort or work done to perform the activity).[38] Intensity is measured as absolute or relative intensity. Absolute intensity is the rate of work performed and does not account for individual fitness to perform the work. In contrast, relative intensity accounts for an individual cardiorespiratory fitness level to

perform the work. Relative intensity is measured as perceived exertion, percent of aerobic capacity (VO_{2max}), or percent of maximum heart rate.[38] The absolute intensity of physical activities is expressed as the rate of energy expenditure and metabolic equivalent of task (MET) is widely used to measure intensity.[39] A MET is the ratio of the rate of energy expended during an activity to the rate of energy expended at rest while awake, which is equivalent to 1 MET. [39] Physical activities have been classified into three intensity levels – light (1.1 – 2.9 METs), moderate (3.0 – 5.9 METs), and vigorous ($\geq$ 6.0 METs). For example, a brisk walk at 3 miles per hour expends 3.3 METs and is classified as a moderate intensity activity. If a person engages in 30 minutes of a 3.3 MET activity (30 minutes X 3.3 METs) then 99 MET-minutes have been expended. Table 3 includes examples of types of physical activities by intensity level. The use of absolute intensity provides a standardized way to measure physical activity intensity across populations and studies, and to measure associations of physical activity with health outcomes.[38]

Table 3. Types of activities according to their MET values.

Type of Intensity	Types of Activities [40]
Light intensity 1.1 – 2.9 METs	Light effort in household tasks like mopping, standing, cleaning, sweeping, carrying out trash, washing dishes; stretching; yoga (Hatha)
Moderate intensity 3.0 – 5.9 METs	Walking; household activities with moderate effort; light moderate effort gardening like digging, spading; mowing lawn with moderate effort; weight training; pilates; water aerobics; yoga (Power)
Vigorous intensity $\geq$ 6.0 METs	Running, bicycling, general aerobic dance, rowing

In 2008 and 2018, the US Department of Health and Human Services released physical activity guidelines for all Americans. Based on their review of the physical activity literature, substantial health benefits were achieved with 500 to 1,000 MET-minutes per week (8.3 to 16.7 MET-hours per week) of aerobic physical activity.[39, 41] The committee concluded there was a dose response relationship so that some health benefits were observed for less than 500 MET-

minutes and more benefits were observed for more than 1,000 MET-minutes. The committee put forth the recommendation for adults for aerobic physical activity to engage in at least 150 minutes per week of moderate intensity or 75 minutes of vigorous intensity, or the equivalent combination.[39, 41] The committee also suggested that for additional health benefits adults should engage in 300 minutes of moderate intensity per week or 150 minutes of vigorous intensity or the equivalent combination of moderate and vigorous activity.

Below is a table that summarizes how walking at 3.3 METS following the guidelines translates into minutes spent per day, MET-minutes per week, and MET-hours per week (Table 4). Throughout the physical activity literature, different metrics are used and this table can be helpful for interpreting different specifications of physical activity.

Table 4. How walking at 3.3 METs at different guideline levels translates into minutes per week, minutes per day, MET-minutes per week, and MET-hours per week

	Minutes per week	Minutes per day	MET-minutes per week	MET-hours per week
Minimum amount to meet PAG guidelines	150 min per week	21.4	495	8.25
Double guidelines (additional health benefits per the PAG)	300 min per week	42.9	990	16.5
Triple guidelines	450 min per week	64.3	1485	24.8

Abbreviations: PAG= 2008 physical activity guidelines

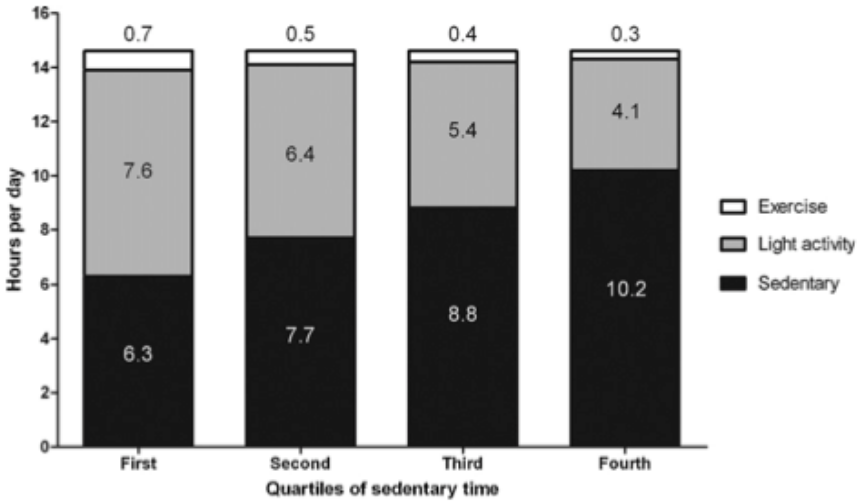
The National Health Interview Survey (2011-2014) asked about leisure time aerobic physical activity. Overall, 49.9% of respondents interviewed (adults ≥ 18 years) reported enough activity to be classified as meeting the aerobic activity federal guidelines.[42] Men were more likely than women to meet the guidelines and whites were more likely than African Americans to meet the guidelines. In examining across gender-race categories, white males were the most likely to meet guidelines (54.1%), followed by African American males (49.6%), white females

(48.4%), and African American females (35.8%).[42] These data were based on self-report of physical activity. Studies that have compared self-report and accelerometer measured physical activity show that the amount of physical activity that is self-reported is higher than objectively measured physical activity.[43, 44] For example, in an analysis of the 2005-2006 NHANES cycle, adults who self-reported meeting guidelines of 150 minutes of moderate-to-vigorous physical activity (MVPA) per week expended approximately 57 minutes a week in MVPA as measured by accelerometer.[43]

3.3.2 Sedentary behavior

Sedentary behavior is distinct from physical activity – sedentary behaviors are any waking behaviors that expend little energy expenditure ($\leq$ 1.5 metabolic equivalent of task (METs)) while in a sitting, reclining, or lying posture.[45, 46] Examples include sitting at work, sitting or lying to watch TV, sitting while commuting, and sitting to do other recreational activities like reading, knitting, or playing cards.[47, 48] Most energy expenditure throughout a day is from light activity (Figure 2) and research suggests that time spent in light activities has been replaced by sedentary behaviors due to environmental and technological changes in society.[48, 49] Time spent in sedentary behavior can be measured as overall sedentary time across a day, the amount of time spent in specific behaviors (TV, computer use), or time occurring in a specific domain (work, leisure, domestic, transport). Often, time spent in sedentary behaviors is collected by self-report questionnaires or activity logs, but also can be estimated from accelerometers.[47]

Figure 2. Accelerometer-measured distribution of time spent in sedentary, light-intensity, and moderate intensity according to quartile of sedentary time, NHANES



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The NHANES 2003-2004 data collection cycle used accelerometers and Matthews et al. estimated total time spent in sedentary behavior using these data.[50] On average, US adults spend 7.7 hours/day in sedentary behavior. The prevalence of sedentary behavior is higher with older age groups. For example, adults 40-49 years spent 7.55 hours per day sedentary, adults 50-59 years spent 7.87 hours per day sedentary, those 60-69 spent 8.41 days sedentary, and those 70-85 years spent 9.28 hours per day sedentary.[50]

One of the most common sedentary behaviors reported by adults is television viewing.[51] On average Americans spend about 3 hours a day watching television. Men spent more time watching TV than women (men weekday 2.71 hours/day, weekend 3.75 hours/day, women

weekday 2.43 hours/day, weekend 2.86 hours/day) and the prevalence is higher for older age groups.[51]

3.4 Epidemiology of physical activity and sedentary behavior with CVD and cancer

The purpose of this dissertation is to examine the association between physical activity and sedentary behavior with years lived free of CVD and cancer. Because of the sparse research in this area, the broader physical activity and sedentary behavior literature will be summarized with respect to the outcomes included in this dissertation. For example, the health expectancy outcomes combine incidence and mortality into a summary measure. Therefore, the literature on physical activity and sedentary behavior with all-cause mortality and incidence of each disease is briefly summarized.

3.4.1 All-cause mortality

3.4.1.1 Physical activity and all-cause mortality

A robust body of evidence provides support that physical activity reduces the risk of all-cause mortality.[52, 53] Multiple sources suggest that the relationship between physical activity and mortality is curvilinear. For example, Arem et al. examined leisure time MVPA and all-cause mortality in an analysis of pooled data from 6 studies in the National Cancer Institute (NCI) Consortium Cohort. These authors illustrated that there was a mortality reduction of 20% (hazard ratio (HR)=0.80 (95% confidence interval (CI) 0.78, 0.82)) even below the recommended guidelines of 7.5 MET-hours per week compared to no activity, a 31% reduction at meeting and doubling guidelines (7.5-<15 MET-hours per week HR=0.69, (95% CI 0.67, 0.70)) and further risk reduction at higher levels of physical activity.[54] Both this study and the review by the 2018 physical activity guidelines committee suggest a curvilinear relationship between level of moderate-to-vigorous physical activity and risk reduction in all-cause mortality, such that a large

benefit is observed at lower levels of activity and then risk reduction continues at higher levels of activity.[41]

Further research suggests that people who engage in more physical activity have a longer life expectancy compared to those who engage in less activity.[55, 56] For example, Moore et al. used the NCI cohorts and examined how different leisure time physical activity levels compared to none were associated with life expectancy: the authors observed at a physical activity level of 0.1-3.74 MET-hours per week a gain of 1.8 years of life (95% CI 1.6, 2.0), at 3.75-7.4 MET-hours per week a gain of 2.5 years, at 7.5-14.9 MET-hours per week a gain of 3.4 years, and a similar increase of 4 years at 15.0-22.4 and ≥22.5 MET-hours per week.[55]

3.4.1.2 Sedentary behavior and all-cause mortality

Meta-analyses and review articles have consistently found an association between greater amounts of sedentary behavior and increased risk of all-cause mortality.[57-59] Biswas et al. included 13 studies and estimated a risk ratio of 1.22 (95% CI 1.08, 1.38) for self-reported high sedentary behavior compared to low with the risk of all-cause mortality (these analyses were adjusted for physical activity).[57] In another meta-analysis six studies were included and examined daily sitting time and observed a hazard ratio of mortality of 1.02 (95% CI 1.01, 1.03) per hour increment in sitting time with adjustment for physical activity. This analysis suggested that the relationship was non-linear because the authors did not observe an increased risk per hour of sitting time at ≤ 7 hours per day, but then observed an increased risk of 5% for each hour increment at > 7 hours per day.[60]

Evidence suggests that one of the most popular sedentary activities, TV viewing, has been associated with an increased risk of mortality.[61, 62] For example, Sun et al. included ten studies in a meta-analysis and observed a risk ratio (RR) of 1.33 (95% CI: 1.20, 1.47) for high

TV viewing time compared to low TV viewing time with the risk of all-cause mortality.[61] In this meta-analysis, the authors examined the dose response relationship and observed an increased risk for all-cause mortality at about 4 hours per day of TV viewing.

3.4.2 CVD

3.4.2.1 Physical activity and CVD

A large body of evidence supports the beneficial effect of physical activity on reducing the risk of CVD mortality and incidence.[54, 63-65] The dose response relationship of physical activity with CVD suggests a large risk reduction at moving from inactive to some activity. For example, in a meta-analysis on CHD and physical activity, the authors observed for those that met US aerobic physical activity guidelines (approximately 8 MET-hours per week) compared to no aerobic physical activity, a 14% lower risk of CHD (RR=0.86 (95% CI 0.77, 0.96) and for those that met advanced guidelines (about 16 MET-hours per week) a 20% lower risk (RR=0.80 (95% CI 0.74, 0.88).[66] Using almost identical physical activity categories, a meta-analysis on HF observed a 10% lower risk of HF for participants who engaged in about 8.25 MET-hours per week compared to no physical activity (HR=0.90 (95% CI 0.87, 0.92)) and at 16.5 MET-hours per week a 19% reduction in HF risk (HR=0.81 (95% CI 0.77, 0.86)).[67] One recent meta-analysis examined the dose response relationship of physical activity with ischemic stroke and suggested a curvilinear relationship with the largest risk reduction in moving from no activity to some activity and continued risk reduction at higher levels of activity.[68] Other meta-analyses suggest little difference of the relationship between physical activity and stroke subtype.[69, 70] For example, Wendel-Vos et al. (19 studies) observed similar estimates for both hemorrhagic (RR = 0.74 (95% CI 0.57, 0.96)) and ischemic stroke (RR = 0.79 (95% CI 0.69, 0.91)) when comparing highest levels of leisure-time physical activity to the lowest level.[69]

3.4.2.2 Sedentary behavior and CVD

Similar to the findings of the association of sedentary behavior with all-cause mortality, greater amounts of sedentary behavior are associated with increased risk of CVD incidence and CVD mortality. Biswas et al. conducted a meta-analysis and observed for the highest levels of sedentary behavior compared to the lowest level of sedentary behavior a risk ratio of 1.14 (95% CI 1.00, 1.30) and 1.15 (95% CI 1.07, 1.24) for CVD incidence (3 studies) and CVD mortality (7 studies).[57] In another meta-analysis that examined TV viewing and incident CVD (4 studies), the authors observed an increased risk of CVD with more TV viewing per day compared to less.[62] In a more recent analysis Young et al. examined a measure of TV, reading, and sitting at computer time and found an increased risk of incident HF (hazard ratio= 1.27 (95% CI 1.15, 1.41)) in comparing highest levels of sedentary behavior with the lowest levels.[71]

A further examination of the dose response relationship of sedentary behavior with CVD suggests a non-linear relationship. In a meta-analysis (9 cohort studies) of the relationship of sedentary behavior (assessed as self-reported sitting time) increased CVD risk was observed at the highest levels of sedentary behavior (median 12.5 hours/day) (HR=1.14 (95% CI 1.09, 1.19)) but not at intermediate levels of sedentary behavior (median 7.5 hours/day, HR=1.02 (95% CI 0.96, 1.08)) compared to the lowest levels of sedentary behavior (median 2.5 hours/day).[9] The authors further explored continuous measures of sedentary behavior and observed the relationship was non-linear with little increase in risk at less than 10 hours per day but an increased risk starting at more than 10 hours of sedentary behavior per day.[9]

3.4.2.3 Years lived free of CVD

The previous review of how physical activity and sedentary behavior were associated with CVD focused on measures of risk. Health expectancy outcomes estimate years lived in

good and poor health. Currently, three studies have examined physical activity and a health expectancy outcome of years lived with and without CVD. Two studies were conducted with the Framingham cohort [11, 12] and the other report analyzed 3 European cohorts.[10] Of the three studies, two examined how multiple risk factors, including physical activity, influenced years lived with and without CVD [11] [10] and the other study included only physical activity and not other health behaviors.[12]

In both Framingham studies, participants were asked how long they spent in various activities and each activity was assigned a weight based on estimated oxygen consumption to reflect METs: sleeping (weight=1), resting (weight=1.1), or engaged in light (weight=1.5), moderate (weight=2.4), and heavy (weight=5) physical activity. A daily activity score was summed and grouped into tertiles (low =< 30, moderate=30-33, high =>33).[11, 12] In the European study only vigorous physical activity was assessed with a question on participating in any vigorous activity at least once per week to cause increased breathing or sweating.[10] Across the three studies, assessment of CVD was similar and is summarized in Table 5.

All studies estimated life expectancy at age 50. Across all studies, participants who engaged in more physical activity had longer life expectancy, more years free of CVD, and more years lived with CVD compared to participants who engaged in less physical activity. For both men and women, the largest portion of life expectancy was spent as CVD-free. In all the studies, women had longer life expectancy than men. Although women had longer life expectancy, the difference in the number of years lived CVD-free by physical activity level was similar for both genders. For example, Franco et al. [12] estimated that men who engaged in high levels of physical activity could expect to live 22.8 years (95% CI 21.6, 23.9) free of CVD, which was 3.2 years (95% CI 1.9, 4.3) more than men who engaged in low levels of physical activity (19.7 years

CVD-free (95% CI 18.7, 20.6)) (Table 6). Women who engaged in high levels of physical activity could expect to live 29.4 years (95% CI 28.2, 30.6) free of CVD, which was 3.3 (95% CI 2.0, 4.5) more years than women who engaged in low levels of physical activity (26.1 years CVD-free (95% CI 25.3, 27.0)).[12] In both of the other studies [10, 11], similar associations were observed in which the difference in CVD-free life expectancy by physical activity level was similar for both men and women.

These studies are promising in their examination of how years spent free of CVD can be attained by engagement in physical activity. However, there are limitations of this research to consider. The Framingham studies [11, 12] used a physical activity measurement that weights activities by intensity, giving greater weight to high intensity, but the results do not provide the number of MET hours per week associated with CVD-free years, which is easier to interpret. O'Doherty et al. [10] asked only about vigorous activity, but prevalence estimates suggest that a low proportion of people engage in vigorous activity.[44] It would be more informative to know how MET hours per week spent in both moderate and vigorous intensity activity influence disease free years. The two studies conducted in the US were with the Framingham cohort [11, 12], which is primarily white. Although 80% of US adults 65 and older are non-Hispanic white, the ethnic and racial diversity of older adults is projected to increase.[72] It is necessary to include a more diverse population in these types of studies to provide research on how to increase years spent in good health for a range of racial and ethnic older adults.

Although two of these studies [10, 11] included other behaviors that are linked to CVD (such as smoking, obesity, and alcohol), none of these studies examined sedentary behavior. Given the consistent evidence of how sedentary behaviors are linked to an increased risk of CVD, and the

large amount of time people spend in sedentary behaviors, this is another behavior that may influence years spent CVD-free.

Table 5. Summary of studies of physical activity with CVD-free life expectancy

Author, Year	Study Population and Design	Assessment of Physical Activity	Assessment of CVD and death	Findings
Franco 2005 [12]	Framingham, 28 - 62 years; N=9033, prospective cohort	Self-report of time spent per day in at various activities; weights like METS applied, daily score summed and categorized into tertiles	Death, incident and fatal CVD: CHD (angina, coronary insufficiency, MI, sudden or not sudden death), HF, stroke, transient ischemic attack, intermittent claudication; assessed by committee of physicians	For men & women, higher amounts of PA associated with longer LE and years CVD-free Women had longer LE then men; but the difference in LE & CVD free years between high vs. low PA was similar by gender
Nusselder 2009 [11]	Framingham, 28 - 62 years; N=9304, prospective cohort	Self-report time spent per day in at various activities; weights like METS applied, daily score summed and categorized into tertiles	Death, incident and fatal CVD: CHD (angina, coronary insufficiency, MI, sudden or not sudden death), HF, stroke, transient ischemic attack, intermittent claudication; assessed by committee of physicians	For men & women, higher amounts of PA associated with longer LE and years CVD-free Women had longer LE then men but the difference in LE & CVD free years between high vs. low PA was similar by gender
O'Doherty 2016 [10]	3 prospective cohorts from CHANCES[a]; N varies for each study, all age 50+	Self-report of any vigorous activity at least once a week to cause increased breathing/sweating	Death from death register; CVD as acute coronary event or stroke	For men & women, higher amounts of PA associated with longer life expectancy and years CVD-free Women had longer LE then men but the difference in LE & CVD-free years between vigorous vs. no vigorous PA was similar by gender

[a]Three cohorts from the Consortium on Health and Ageing Network of Cohorts in Europe and the United States (CHANCES) were included in the O'Doherty analysis. These include a cohort from the Research Centre for Prevention and Health (RCPH) in Denmark, the ESTHER study a population-based cohort based in the state of Saarland, Germany, and a cohort from the municipality of Tromsø, Norway. Abbreviations: CHANCES= Consortium on Health and Ageing Network of Cohorts in Europe and the United States; CHD= coronary heart disease, CVD= cardiovascular disease, HF= heart failure, LE= life expectancy, MET= metabolic equivalent of task, MI= myocardial infarction, PA= physical activity

Table 6. Estimates of total life expectancy and CVD-free life expectancy by level of physical activity.

	Total LE at age 50, years (95% CI)	Difference, years (95% CI)	LE free of CVD at age 50, years (95% CI)	Difference, years (95% CI)
Franco 2005, men[a]				
high PA	29.9 (29.0, 31.0)	3.7 (2.6, 4.8)	22.8 (21.6, 23.9)	3.2 (1.9, 4.3)
medium PA	27.6 (26.6, 28.7)	1.3 (0.3, 2.3)	20.8 (19.6, 21.9)	1.1 (-0.02, 2.1)
low PA	26.2 (25.4, 27.1)	ref	19.7 (18.7, 20.6)	ref
Franco 2005, women[a]				
high PA	36.0 (35.0, 37.1)	3.5 (2.4, 4.6)	29.4 (28.2, 30.6)	3.3 (2.0, 4.5)
medium PA	34.0 (33.0, 35.0)	1.5 (0.4, 2.5)	27.4 (26.4, 28.5)	1.3 (0.1, 2.4)
low PA	32.5 (31.7, 33.3)	ref	26.1 (25.3, 27.0)	ref
Nusselder 2009, men[b]				
high PA	30.0 (29.0, 31.0)	3.5 (2.5, 4.6)	22.8 (21.7, 23.9)	3.0 (1.8, 4.3)
medium PA	27.7 (26.8, 28.8)	1.3 (0.3, 3.2)	20.8 (19.7, 22.0)	1.1 (0.0, 2.2)
low PA	26.4 (25.7, 27.3)	ref	19.7 (18.9, 20.6)	ref
Nusselder 2009, women[b]				
high PA	36.1 (35.0, 37.2)	3.4 (2.3, 4.5)	29.4 (28.2, 30.6)	3.1 (1.9, 4.3)
medium PA	34.1 (33.2, 35.1)	1.5 (0.5, 2.5)	27.6 (26.6, 28.7)	1.3 (0.2, 2.4)
low PA	32.7 (31.9, 33.5)	ref	26.3 (25.5, 27.1)	ref
O'Doherty 2016 RCPH, men[c,d]				
vigorous PA	25.0 (23.2, 26.9)	3.1 (1.4, 5.1)	22.0 (20.4, 23.9)	2.5 (0.8, 4.3)
no vigorous PA	21.9 (20.9, 22.8)	ref	19.5 (18.5, 20.4)	ref
O'Doherty 2016 RCPH, women[c,d]				
vigorous PA	29.5 (27.1, 31.7)	3.5 (1.4, 5.4)	26.4 (24.3, 28.5)	2.9 (0.9, 4.8)
no vigorous PA	26.0 (24.8, 27.3)	ref	23.5 (22.4, 24.9)	ref
O'Doherty 2016 ESTHER, men[c,d]				
vigorous PA	34.8 (31.7, 40.4)	6.8 (4.3, 10.7)	27.0 (25.8, 28.3)	4.3 (3.0, 5.7)
no vigorous PA	28.1 (26.3, 31.2)	ref	22.7 (21.7, 23.6)	ref
O'Doherty 2016 ESTHER, women[c,d]				
vigorous PA	42.3 (38.6, 47.4)	6.9 (4.5, 9.9)	34.8 (33.1, 36.6)	4.8 (3.3, 6.4)
no vigorous PA	35.3 (33.1, 39.0)	ref	29.9 (28.9, 31.1)	ref
O'Doherty 2016 Tromsø, men[c,d]				

	Total LE at age 50, years (95% CI)	Difference, years (95% CI)	LE free of CVD at age 50, years (95% CI)	Difference, years (95% CI)
vigorous PA	27.8 (27.1, 28.4)	3.2 (2.4, 3.9)	23.0 (22.4, 23.7)	2.5 (1.7, 3.2)
no vigorous PA	24.6 (24.0, 25.1)	ref	20.6 (20.0, 21.1)	ref
O'Doherty 2016 Tromsø, women[c,d]				
vigorous PA	32.6 (31.7, 33.4)	3.5 (2.7, 4.3)	28.9 (28.1, 29.7)	2.9 (2.1, 3.8)
no vigorous PA	29.1 (28.6, 29.5)	ref	26.0 (25.5, 26.5)	ref

[a]Franco et al. controlled for age, sex, smoking, exam date, and comorbidity at baseline (cancer, diabetes, left ventricular hypertrophy, arthritis, ankle edema or any pulmonary disease).

[b]Nusselder et al. estimates controlled for comorbidity at baseline (cancer, diabetes, left ventricular hypertrophy, arthritis, ankle edema or any pulmonary disease), exam date, and smoking.

[c]O'Doherty et al. controlled for age, history of diabetes, hypertension, total/HDL cholesterol ratio, smoking, BMI, alcohol.

[d]Three cohorts from the Consortium on Health and Ageing Network of Cohorts in Europe and the United States (CHANCES) were included in the O'Doherty analysis. These include a cohort from the Research Centre for Prevention and Health (RCPH) in Denmark, the ESTHER study a population-based cohort based in the state of Saarland, Germany, and a cohort from the municipality of Tromsø, Norway.

Abbreviations: CI= confidence interval, CVD= cardiovascular disease, LE= life expectancy, PA= physical activity

3.4.3 Cancer

3.4.3.1 Physical activity and cancer

In 2007 the World Cancer Research Fund (WCRF) and American Institute for Cancer Research (AICR) reviewed literature on the epidemiological evidence of the association of physical activity and cancer.[73] This report concluded that physical activity was associated with a lower risk of colon cancer, postmenopausal breast cancer, and endometrial cancer. A recent meta-analysis [7] included 26 types of cancer and observed that high levels of physical activity compared to low levels was associated with a lower risk for 13 types of cancer (esophageal adenocarcinoma, liver, lung, kidney, gastric cardia, endometrial, myeloid leukemia, myeloma, colon, head and neck, rectal, bladder, and breast).

Consistent findings suggest physical activity is protective against breast cancer but may vary by menopausal status. A recent meta-analysis by Wu et al. [74] included 31 studies and observed a risk ratio of 0.87 (95% CI 0.83, 0.92) for highest compared to the lowest level of total physical activity for the risk of breast cancer. When separately examining premenopausal and postmenopausal breast cancer, the Wu et al. meta-analysis [74] and the Continuous Update Report (CUP) [75] (conducted by WCRF and AICR) review observed similar estimates for postmenopausal breast cancer (Wu et al. RR=0.87 (95% CI 0.87, 0.92), CUP review RR=0.87 (95% CI 0.7, 0.96)). These two reviews had inconsistent results about premenopausal breast cancer - Wu et al. observed a strong association but the CUP review observed a weak association. [74, 75]

Consistent evidence suggests that physical activity is beneficial at reducing the risk of colon cancer. In a meta-analysis of 22 prospective cohort studies, the authors observed a risk ratio of 0.83 (95% CI 0.78, 0.88) for the highest level of physical activity compared to lowest

level with the risk of colon cancer.[76] Similar estimates were observed for men (RR=0.76 (95% CI 0.71, 0.82)) and women (RR=0.79 (95% CI 0.71, 0.88)).[76] In studies that separately examined physical activity with colon and rectal cancers, strong association were observed for colon cancer but not rectal.[77]

The findings on the association of physical activity with prostate cancer risk have suggested a weak relationship. Liu et al. conducted a meta-analysis of 19 cohort studies and observed weak protective associations for risk of prostate cancer by level of physical activity (RR=0.95 (95% CI, 0.90, 1.00).[78] The CUP report in 2014 found similar estimates as Liu et al.[79]. With the NCI Cohort Consortium Moore et al. estimated an HR of 1.05 (95% CI 1.03. 1.08)) for the highest level of physical activity compared to lowest levels for risk of prostate cancer.[7] The findings for how these relationships vary by race has been mixed. For example, Liu et al. estimated weaker association for whites (RR=0.98 (95% CI 0.93, 1.04)) and much stronger associations for African Americans (RR=0.62 (95% CI 0.24, 1.61)) but this estimate was based on two studies.[78] However, in Moore et al. the authors observed no difference by race.[7]

In a recent meta-analysis by Zhong et al. on physical activity and incident lung cancer, 18 studies were included and physical activity was inversely associated with a reduced risk of lung cancer.[80] Compared to low levels of physical activity, the authors observed a risk ratio of 0.87 (95% CI 0.84, 0.90) for moderate levels of activity and a risk ratio of 0.75 (95% CI 0.68, 0.84) at high levels of activity for the risk of lung cancer.[80] In a pooled NCI cohort analysis, similar associations were observed for the inverse association of physical activity with incident lung cancer.[7]

3.4.3.2 Sedentary behavior and cancer

Consistent evidences suggests that higher amounts of time spent in sedentary behavior are associated with an increased risk of certain cancers compared to lower amounts of time spent in sedentary behavior.[8, 81, 82] In comparing the highest to lowest levels of sedentary behavior (43 studies) a meta-analysis observed an increased risk for colon cancer (RR=1.28 (95% CI 1.13, 1.45)), endometrial cancer (RR=1.36 (95% CI 1.15, 1.60)), and lung cancer (RR=1.21 (95% CI 1.03, 1.43)) and weak associations for breast cancer (RR=1.03; (95% CI 0.95, 1.12)), prostate cancer (RR=1.10 (95% CI 0.93, 1.30)) and others (ovarian, gastric, esophageal, testicular, renal cell, and non-Hodgkin lymphoma).[8] While this review noted weak findings for breast cancer, another meta-analysis noted an increased risk for breast cancer (RR=1.17 (95% CI 1.03, 1.33) for high compared to low sedentary behavior.[81]

Fewer studies have been conducted with a measure of TV viewing as a proxy indicator for sedentary behavior. The results have been mixed. For lung cancer, two studies have been conducted and one observed an increased risk for lung cancer for men at viewing TV for four hours or more (RR=1.36 (95% CI 1.04, 1.79)) but null findings were observed with women (RR=1.01 (95% CI 0.66, 1.59))[83] and the other study, among a cohort of non-smokers, had null findings comparing TV viewing time of 5 hours or more to less than 3 hours per day (RR=1.06 (95% CI 0.77, 1.46)).[84] For prostate cancer, one study has been conducted and the authors observed null findings comparing 7 hours of viewing versus less than 1 hour per day. [85] A recent meta analysis included 6 studies on TV viewing time with breast cancer risk and observed null findings (RR=1.07 (95% CI 0.96, 1.20).[86] A meta-analysis that included two studies on TV viewing and examined the risk of colon cancer found a risk ratio of 1.54 (95% CI 1.19, 1.98)[8] for the highest level of TV viewing compared to the lowest levels. Similarly, a recent study with the

UK Biobank cohort observed in comparing ≥ 5 hours of TV viewing a day with ≤ 1 hour a day an increased risk of colorectal cancer (RR=1.32, 95% CI 1.04, 1.68). [87]

3.4.3.3 Years lived free of cancer

To date, none of the health expectancy studies have included cancer as an outcome, although cancer is one of the leading causes of death. Consistent evidence suggests that physical activity and sedentary behaviors are linked to cancer suggesting that this is another area that should be examined on how to increase years spent in good health.

3.4.4 Summary

In summary, physical activity is consistently found to reduce the risk of all-cause mortality, and the incidence of CVD and certain cancers. Also, higher amounts of sedentary behavior are found to increase the risk of mortality, CVD, and certain cancers. The research on how these behaviors are related to health expectancy outcomes, such as years lived free of CVD and cancer, is sparse. Currently, three studies exist on physical activity and CVD outcomes, but no studies have been conducted with sedentary behavior or with cancer outcomes. This dissertation does address many of the limitations (measurement of physical activity, no sedentary behavior measurement, and no cancer outcomes) in the physical activity and health expectancy literature.

3.5 Biological mechanisms of physical activity and sedentary behavior with CVD and cancer

3.5.1 Physical activity and CVD

Physical activity improves many of the risk factors that are shared across cardiovascular diseases. Physical activity is associated with reduced adiposity, improved blood pressure, prevention of diabetes, and improvement in lipid profiles.[31, 37] In addition to influencing CHD

through risk factors, the hypothesized mechanisms for how physical activity is related to CHD are related to an increase in myocardial oxygen supply and decrease myocardial work and oxygen demand.[31] Physical activity helps maintain a normal blood supply to the heart by lowering blood cholesterol, thereby decreasing the risk of atherosclerosis. Physical activity also lowers heart rate and blood pressure at rest and during exercise, which influence the oxygen demand of the heart.[37] Another potential mechanism includes a reduced risk of thrombosis due to an expansion of plasma volume, which should reduce thickness of the blood and reduce platelet stickiness.[37] Many of the hypothesized mechanisms for how physical activity influences CHD are also hypothesized for stroke. Physical activity reduces the risk of developing atherosclerosis and thrombosis, which usually develop before a stroke occurs. In addition to physical activity improving many of the CVD risk factors that develop before HF develops, physical activity has also been linked to improved cardiac physiological changes. These types of changes include improved left ventricular mass, reduced arterial stiffness, and improved left ventricular diastolic function. These observations have been observed with athletes as well as in community-dwelling population based studies of adults.[88]

3.5.2. Sedentary behavior and CVD

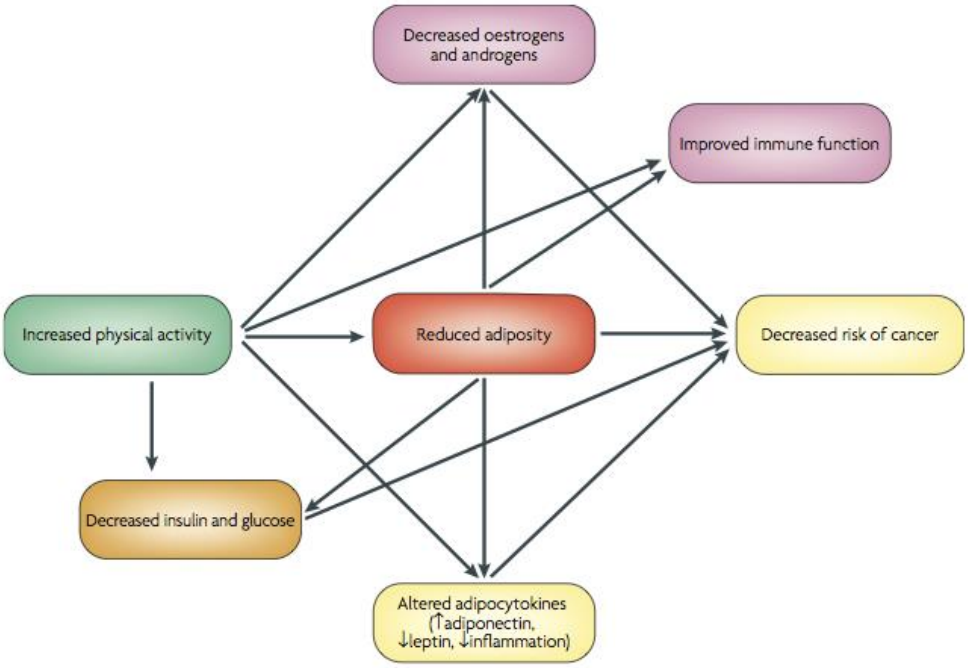
Higher levels of time spent in sedentary behavior are associated with development of many CVD risk factors including obesity, elevated blood glucose, and type 2 diabetes.[48] Sedentary behavior may displace time spent in light intensity activities.[48] Light intensity activities include activities such as walking slowly, cooking, and cleaning. Engagement with more light intensity activity has been associated with better waist circumference, better triglycerides, and improved insulin sensitivity.[89]

In addition to affecting CVD risk factors and displacing light intensity activities, a mechanism that affects glucose and high density lipoprotein cholesterol (HDL-C) production, has been proposed for how sedentary behavior influences cardio-metabolic health.[48, 90] During episodes of prolonged sitting, large skeletal muscles do not contract and lipoprotein lipase (LPL) activity is reduced. LPL activity is essential for glucose and lipid uptake and HDL-C production. Experimental studies with rodents suggest that imposed sedentary behavior decreases LPL activity in red oxidative muscle sections and white glycolytic sections.[90] In contrast, vigorous activity such as running, increased LPL activity in white muscle sections but not the red muscle sections.[90] These findings suggest there may be a distinct pathway for how time spent in sedentary behavior affects skeletal muscle LPL activity in large postural muscles. These changes in LPL activity may influence cardio-metabolic health independent of the amount of physical activity that can increase LPL activity.

3.5.3. Physical activity and cancer

Physical activity may reduce the risk of many cancers through multiple pathways including adiposity, sex hormones, insulin, inflammation, and immune function (Figure 3).[91]

Figure 3. Biological mechanisms for how physical activity may reduce cancer risk



Reprinted by permission from Springer Nature: *Nature Reviews Cancer,* Mechanisms linking physical activity with cancer, McTiernan A, (2008).

Physical activity may reduce the risk of many cancers by reducing adiposity. Adiposity influences the production of many growth factors, such as insulin, insulin-like growth factor 1 (IGF-1), and leptin, and these factors are suggested to promote the growth of cancer cells.[73] The adipose tissue is also the site of estrogen synthesis in men and postmenopausal women.[73] Higher levels of adiposity are related to higher levels of estrogen and increased conversion of androgens to estrogen which are linked to increased risk of certain cancers.[37] The adipose tissue produces inflammatory markers including tumor necrosis factor (TNF) alpha, interleukin (IL)-6, and C-reactive protein. These markers may promote cancer development.[73] Therefore, physical activity may reduce adipose tissue and in turn lower levels of inflammatory markers, estrogens and

testosterone, and improve insulin sensitivity.[91, 92] Cancers potentially associated with this mechanism include colon, postmenopausal breast, endometrium, and ovary. [91, 92]

Regarding the hypothesized insulin sensitivity pathway, physical activity improves insulin sensitivity, lowers plasma insulin, and lowers glucose levels.[92] These changes may be due to reduced body fat, increased skeletal muscle mass, and increased glucose transport into muscles. Cancers possibly associated with this mechanism include colon, breast, endometrium, ovary, and prostate.[91, 92]

Another pathway in which physical activity may reduce cancer risk is through lowering levels of estrogens and androgens. This is particularly important for breast and endometrial cancers.[91] Women with higher levels of estrogens and androgens have a higher risk of developing breast and endometrial cancer.[34] Observational research suggests active premenopausal women and athletes have delayed age at menarche, fewer ovulatory cycles, and lower levels of estrogen and progesterone. These factors would contribute to lower life-time estrogen and progesterone levels that affect the risk of breast and endometrial cancer.[91] For postmenopausal women, the main source of estrogen is not from the ovaries but from adipose tissue. Research suggests that physical activity helps lower estrogen levels for postmenopausal women, which is likely due to physical activity reducing body fat.[91] For men, the results are inconclusive whether physical activity reduces levels of androgens and the relationship between androgens and prostate cancer is unclear.[34, 91] Cancers associated with this mechanism include breast, prostate, and endometrial cancers.[91]

Physical activity may reduce systematic inflammation by lowering levels of inflammatory markers like C-reactive protein, interleukin 6, and tumor necrosis factor-alpha. These changes may be partly due to fat loss.[91] Physical activity may enhance immune function

by increasing levels of immune cells in blood (natural killer cells, lymphocytes, monocytes, neutrophils) that respond to recognizing and eliminating cancerous cells.[91, 92] Both the inflammation and immune pathways may affect most cancers.[91]

Other hypothesized mechanisms potentially related to colon cancer consider that physical activity may increase gut motility and decrease bowel transit time. This could reduce the time potential carcinogens are in contact with the lining of the bowel.[91, 92]

3.5.4. Sedentary behavior and cancer

Most of the hypothesized mechanisms for how sedentary behaviors are associated with cancer development focus on the same pathways in which physical activity may reduce cancer risk. As previously mentioned, adiposity is a risk factor for developing many cancers and research suggests that high levels of sedentary behavior are associated with increased adiposity.[48, 58] Similarly, high levels of sedentary behavior are associated with increased risk of type 2 diabetes and elevated blood glucose.[48, 59] Increased levels of glucose and insulin resistance are hypothesized to be risk factors for some cancers. Other pathways that may be involved include high levels of sex hormones and inflammation, and low levels of vitamin D [93] but the evidence linking sedentary behavior to these pathways is very limited.[93]

3.6 Summary

Chronic diseases are the leading cause of death, premature mortality, and years lived with disability in the US.[1, 2] Although chronic disease mortality rates have declined and life expectancy has increased, many adults are living longer in poor health.[2] In 2010, the average US life expectancy at birth was 78.2 years but adults could expect to live at least 10 years with illness and disability.[2] CVD and cancer are the major contributors to the chronic disease burden and the two leading causes of death.[3] The major CVDs are CHD, stroke, and HF [4] and some of

the leading cancers are breast, prostate, lung, and colorectal.[5] Two modifiable behaviors linked to all these diseases are physical activity and sedentary behavior. Consistent epidemiological evidence suggests physical activity prevents CHD, stroke, HF, postmenopausal breast cancer, colorectal cancer, lung cancer, and prostate cancer.[6, 7] Conversely, sedentary behavior is linked to increased risk of these diseases.[8, 9] Three studies suggest that engaging in physical activity can increase the number of years spent free of CVD.[10-12] This research is promising for increasing years spent in good health but limited in a number of ways: the studies have used physical activity measurements that are hard to generalize across populations, have not included cancer outcomes, and have not examined sedentary behaviors.

By 2030 Americans age 65 and older will account for 20% of the US population and currently two out of three Americans in this age group have multiple chronic conditions.[72] Identifying behaviors that can extend healthy years is a priority for older adults as this population is projected to grow.[13] The goal of this dissertation is to fill many of the gaps in the existing physical activity, sedentary behavior, and health expectancy literature and to further inform how to increase years spent in good health. This research set out to provide estimates of years expected to live free of CVD and cancer by common lifestyle behaviors by investigating the following aims 1) to evaluate the association of leisure-time physical activity with life expectancy free of disease for 3 CVDs and 4 cancers; and 2) to evaluate the association of TV viewing with life expectancy free of the same diseases.

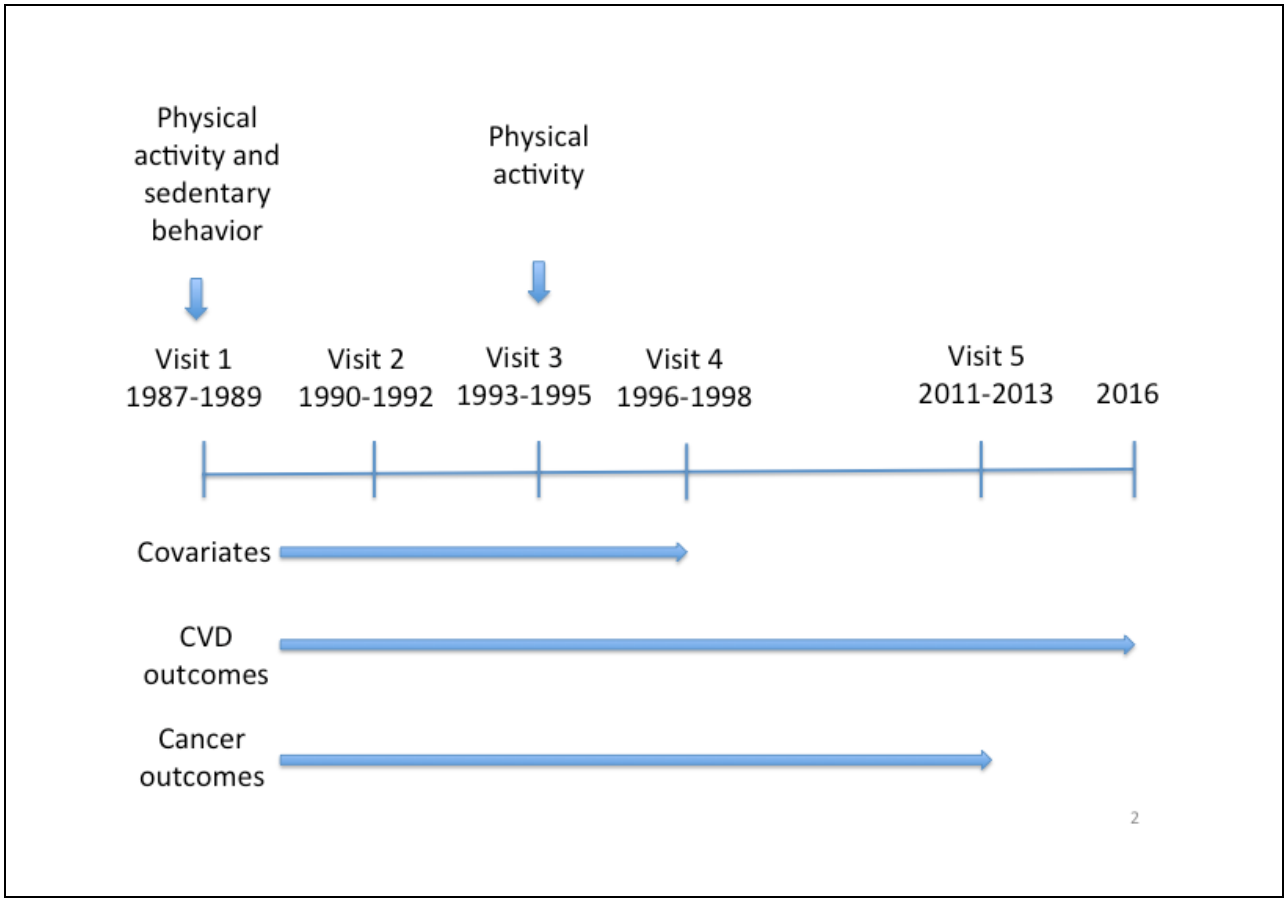
CHAPTER 4: OVERARCHING RESEARCH METHODS

4.1 Study population and study design

All dissertation analyses were conducted using data from the Atherosclerosis Risk in Communities (ARIC) study. The ARIC study is a population-based prospective cohort of 15,792 mostly white and African-American adults age 45 – 64 years that began in 1987 - 1989 in four geographic areas in the US (Forsyth County, North Carolina; Jackson, Mississippi; Washington County, Maryland; and Minneapolis, Minnesota). The study is ongoing and has conducted six examination visits (Visit 1 1987-89, Visit 2 1990-92, Visit 3 1993-95, Visit 4 1996-98, Visit 5 2011-13, and Visit 6 2016-17). Cohort members were asked to participate in interviews, clinical examinations, and annual telephone follow-up interviews.[94]

All analyses used the prospective cohort design of the ARIC Study (Figure 4). Physical activity was measured at Visit 1 (1987-89) and Visit 3 (1993-95) and TV was measured at Visit 1. The following disease outcomes were ascertained from Visit 1 through 2016: CHD, stroke, and HF; and the cancer outcomes were ascertained from Visit 1 through 2012: postmenopausal breast cancer, prostate cancer, lung cancer, and colorectal cancer.

Figure 4. Schematic of study design



4.1.1 CVD analysis exclusions

Of the 15,792 ARIC participants examined at baseline, for the CVD analysis we excluded participants with prevalent CVD (having prevalent CHD, stroke, or HF) (n=2,023), and participants who experienced a CVD event (CHD, stroke, or HF) or death within the first year of follow-up (n=132). Asian or American Indian/Alaskan Indian participants (n=48) and African American participants in Minnesota and Washington County (n=55) were excluded due to small numbers. After exclusions, the analytic set comprised 13,534 (86%) participants.

4.1.2 Cancer analysis exclusions

Of the 15,792 ARIC participants examined at baseline, for the cancer analysis we excluded participants who did not consent to non-cardiovascular disease research (n=149), those with prevalent cancer at baseline (n=902), and those who experienced cancer (colorectal, lung, prostate, or breast) or death within the first year of follow-up (n=130). We also excluded Asian and American Indian/Alaskan Indian participants (n=48) and African American participants in Minnesota and Washington County (n=55) due to small numbers at these sites. After exclusions, 14,508 (92%) participants were included in analysis for colorectal and lung models, 6,582 men for prostate models and 7,849 women for postmenopausal breast models (77 women were not included in breast cancer models because they died or developed breast cancer before reaching menopause).

4.2 Outcomes

4.2.1 CVD outcomes

We separately examined incident nonfatal CHD, stroke, and HF. Prevalent CHD at baseline was defined as a myocardial infarction (MI) from Visit 1 ECG data, or a self-reported history of MI or coronary revascularization. Incident nonfatal CHD was defined as definite or probable MI, silent MI between examinations detected by electrocardiography, and cardiac revascularization procedures. MI events were identified from active surveillance of hospitalizations occurring among ARIC cohort members.[95, 96] Trained study personnel abstracted clinical information from the medical records of eligible hospitalizations. Definite or probable MI was defined from a diagnostic algorithm based on chest pain, electrocardiograms, and cardiac enzyme data.[95] A committee reviewed all CHD events and disagreements were adjudicated.

Prevalent stroke at baseline was defined as self-reported history of a stroke or transient ischemic attack. Incident nonfatal stroke events were identified by self-report from ARIC Visit examinations, annual follow-up telephone calls, and active surveillance of hospitalizations in the ARIC communities.[97] A trained nurse abstracted the medical record if a hospitalization had stroke diagnostic codes, if discharge summaries contained stroke related keywords, if neuroimaging had cerebrovascular findings, or if the patient had been admitted to the neurological intensive care unit.[97] Stroke events were classified as definite or probable by computer algorithm and by a physician reviewer according to criteria adapted from the National Survey of Stroke.[97, 98] A second physician adjudicated disagreements.

Prevalent HF at baseline was defined as self-report of taking a medication for HF in the past two weeks or a score of three on the Gothenburg criteria.[99] Incident nonfatal HF was identified by active surveillance of hospitalizations with ICD-9 code 428.xx in any position and relevant ICD-10 codes. Medical records of eligible hospitalizations that occurred after 2004 were abstracted and independently reviewed by two trained and certified physicians on the ARIC HF Classification Committee.[100]

4.2.2 Cancer outcomes

First primary invasive cancer diagnoses (postmenopausal breast, prostate, lung, and colorectal) were ascertained by linkage with statewide cancer registries from 1987 through December 31, 2012.[101] Some of the state cancer registries were not complete or established at the start of the ARIC study, and for this time period cancer cases were identified by surveillance of hospital discharge summaries in the ARIC Study regions and confirmed with medical record abstraction.[101] The ARIC Cancer Coordinating Center adjudication teams adjudicated all

potential cancer cases.[101] Participants were considered to have prevalent cancer at Visit 1 if they been told by a doctor that they had cancer.

4.2.3 All-cause mortality

All-cause mortality was included as an outcome for both the CVD and cancer analyses. Deaths were ascertained from cohort entry until December 31, 2012 for the cancer analysis and until December 31, 2016 for the CVD analysis. Deaths were identified by annual phone calls, active surveillance of hospitalizations in ARIC communities, and linkage with the National Death Index. Death certificates were reviewed by medical abstractors to determine underlying causes of death and confirmed with family members.[94, 95]

4.3. Exposures

Leisure-time physical activity was included in both the CVD and cancer analysis. At Visits 1 and 3 participants were asked with the Baecke questionnaire to report up to four leisure-time physical activities they participated in the past year.[102, 103] For each activity, the number of hours/week (duration) and months/year (frequency) were reported and a metabolic equivalent (MET) value was assigned based on the Compendium of Physical Activities.[104] Activities with a MET value of 3 or higher were classified as moderate to vigorous intensity.[38] The MET, frequency, and duration of each activity were used to calculate MET hours per week (MET-h/week) spent in leisure-time moderate-to-vigorous physical activity (LTPA). MET-h/week spent in LTPA at Visits 1 and 3 was categorized as none, < median (0.1 – <13.2 MET-h/week), and ≥ median (13.2+ MET-h/week). The cut point was based on the Visit 1 median value of MET-h/week among those who reported any LTPA. The LTPA distribution was very similar for the CVD and cancer analyses and the same categories were used for both analyses.

Sedentary behavior, any waking behavior that expends little energy expenditure (≤ 1.5 METs) while in a sitting or reclining posture,[45] was assessed with a question on TV viewing. Participants were asked at Visit 1 how often they viewed TV and classified as never/seldom, sometimes, and often/very often. TV was specified with same categories for both the CVD and cancer analyses

4.4. Covariates

In both CVD and cancer analyses, we included the following socio-demographic factors - age, race by ARIC study field center (white Forsyth County, African American Forsyth County, white Washington County, white Minneapolis, African American Jackson), gender, and education (high school or less, vocational school, some college or college degree, higher than college degree).

Covariates used in both the CVD and cancer analyses that were assessed at all examination visits included smoking status (never, former, and current smoker), alcohol intake, and body mass index (BMI). Alcohol intake (no current intake, ≤ 100g, and > 100g)[105] was obtained by asking participants to report their usual intake of alcoholic beverages of a standard serving of wine, beer, and hard liquor per week. Weekly alcohol intake was derived as the sum of the alcohol amount of each type of drink (4 ounce glass of wine=10.8 grams (g), 12 ounces of beer=13.2g, 1.5 ounce of hard liquor=15.1g) multiplied by the number of drinks. BMI (weight in kilograms (kg) divided by square of height in meters (m^2)) was calculated from interviewer measured weight and height and participants were classified according to standard BMI categories (underweight/normal <25.0 kg/m^2, overweight 25.0 - < 30 kg/m^2, and obese ≥ 30.0 kg/m^2).[106]

For the CVD analysis, additional covariates ascertained at all examination visits included blood pressure, diabetes, and high density lipoprotein cholesterol (HDL-C). Seated blood pressure after 5 minutes of rest was measured at all visits by a trained technician. The average of the second and third measurement were used. Participants were classified as hypertensive if systolic blood pressure was ≥140 millimeters of mercury (mmHg), or diastolic blood pressure was ≥ 90mmHg, or reported use of antihypertensive medication in the past two weeks. Diabetes status was considered positive if study participants had been told by a physician they had diabetes, or had a fasting plasma glucose ≥126 milligrams per deciliter (mg/dL), or had a non-fasting glucose ≥200 mg/dL, or reported use of hypoglycemic medication in the past two weeks. HDL-C was collected from 12 hour fasting blood samples drawn by venipuncture from an antecubital vein and specified as a continuous variable.

For the cancer analysis, additional covariates included use of menopausal hormone therapy (MHT) and daily serving of red meat. At each visit women self-reported use of MHT (never users, former users of any MHT type, current users of unopposed estrogen, current users of estrogen plus progestin). Habitual dietary intake was collected at Visit 1 with a modified version of a 66-item food frequency questionnaire.[107] Participants were asked how often they ate a serving of a specific food item in the past year. Daily servings of red meat intake was derived based on how often participants reported consuming hamburgers, hot dogs, processed meats, bacon, and beef, pork, or lamb in the past year.

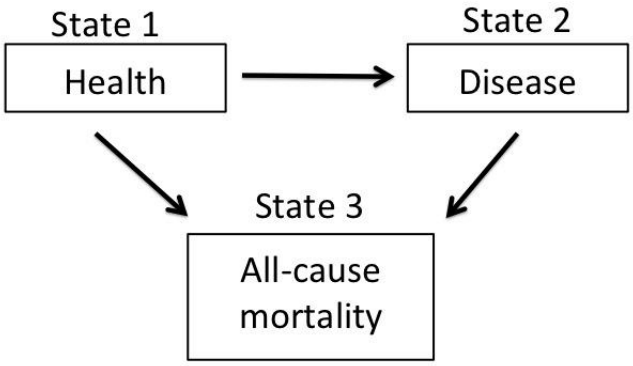
The breast cancer analysis included only postmenopausal women. Women were considered postmenopausal at the ARIC visit in which they reported the following: 1) having both ovaries removed, or 2) if both ovaries had not been removed, they were not taking hormones and had not had a hysterectomy, then they were considered menopausal when they

reported reaching menopause or having no periods in the past two years, or 3) if both ovaries had not been removed but women reported taking hormones, or had a hysterectomy, or did not know their menopause status, then they were considered menopausal when they reached the average cohort race- and smoking status- specific age when menopause was reached (White- Never: 48.3, Former: 47.3 Current: 46.6; African American- Never: 47.8, Former: 47.0, Current: 45.6).

4.5 Statistical analyses

For both the CVD and cancer analyses, multistate survival models were used to estimate how participants moved between health (state 1), disease (state 2), and all-cause mortality (state 3) states (Figure 5). In this model, there were three possible transitions between states– health to disease, health to all-cause mortality, and disease to all-cause mortality. Each type of cancer and CVD was considered the disease state in separate models. For each type of transition, hazard ratios (HR) and 95% confidence intervals (CI) were estimated with the msm R package.[108, 109] The time scale for all models was age; participants started contributing time to the study at the age they entered at Visit 1. For breast cancer analysis, women started contributing time at the age of the visit in which they were considered postmenopausal. For the cancer analysis, follow-up continued until death or end of study (December 31, 2012). For the CVD analysis, follow-up continued until the date of last known contact with each participant, death, or end of study (December 31, 2016). Time-varying covariates closest in time preceding each type of transition were used for the specific transition.

Figure 5. Three state model used in analysis.



We estimated life expectancy at age 50 with the Estimating Life Expectancies in Continuous Time (ELECT) R package separately for men and women.[110] Life expectancy was the expected average number of remaining years of life in health and disease states conditional on reaching age 50 and regardless of health status at age 50. Confidence intervals were estimated using 1000 bootstrap samples. Life expectancy at age 50 was calculated separately for men and women at different levels of LTPA and TV viewing while specifying other covariates used in analytic models to the mean baseline covariate levels of the cohort.

For both the CVD and cancer analyses, we specified models that separately examined LTPA and TV and then specified models that included both LTPA and TV. For all models, confounders included age, gender, race by ARIC center, education, smoking, and alcohol intake.

4.6 Sensitivity analyses

For the CVD analysis, in LTPA models that did not include TV, we also evaluated the impact of additional adjustment for BMI, diabetes status (yes, no), hypertension (yes, no), and HDL-C (continuous) in addition to previously mentioned confounders. The additional covariates

were limited to sensitivity analyses because they could mediate transitions between LTPA from health to disease, health to all-cause mortality, and disease to all-cause mortality.

For the cancer analysis, we examined if results were sensitive to adjustment for BMI by adding it as a covariate to the previously described models in which LTPA and TV were separately examined. Further sensitivity analyses included adding MHT to the breast cancer LTPA model and daily serving of red meat to the colorectal LTPA model.

4.7 Multiple imputation of missing data

For both the CVD and cancer analyses, missing exposure and covariate data at each ARIC Visit were imputed with Multiple Imputation by Chained Equations (MICE).[111, 112] Multiple imputation was conducted separately for the CVD and cancer analyses. For both types of analyses, we imputed 10 datasets and the hazard ratios, standard errors, and life expectancy estimates from each dataset were averaged using Rubin's rule.[113]

Missing exposure and covariate information that occurred when participants either did not answer a question or did not attend an ARIC Visit was imputed with MICE. [111, 114] The percent of missing data ranged from 0.1% to 20% for both the CVD and cancer analysis. The MICE model for both types of analyses included all exposure, covariates, and outcomes used in analytic models, age at each visit, age at each CVD or cancer event, age at death, and characteristics considered to be auxiliary information.[111, 112]

Variables were imputed using a regression method appropriate for their distribution. For both the CVD and cancer analysis, we imputed 10 datasets using a burn-in of 20 iterations before an imputed dataset was drawn. We examined trace plots of continuous variables and compared imputed and observed distributions (frequency distributions for categorical variables and kernel density plots for continuous variables) to assess model convergence. We also conducted a

validation study to measure agreement between imputed and observed values. A 20% random sample of participants who had non-missing exposure and covariate information at each visit were selected for the validation study. For these participants their observed data was set to missing and imputed along with the other participants. After the imputation their imputed values were compared to their observed data with kappa statistics and Pearson and Spearman correlations.

In the CVD analysis we originally included the ARIC Visit 5 variables. The agreement between the imputed and observed values for the Visit 5 variables was poor and we decided to use variables from Visits 1 to 4 in the imputation model and analysis. In the cancer analysis we imputed variables for Visits 1 to 4 due to our study design (the ascertainment of cancer ends in 2012 which is midway through Visit 5). In both the CVD and cancer validation studies, the Visit 3 TV viewing variable did not impute well; the agreement between imputed and observed values was poor. Therefore, we decided to only use a baseline measure of TV viewing for both the CVD and cancer analyses. The validation study suggested good agreement for the other variables.

4.8 Study power

No methods exist to estimate power for multistate models. Therefore, we treated each type of transition in the multistate model (health to disease, health to death, disease to death) as a separate power analysis calculation. Using the Stata Cox proportional hazard power analysis program, we estimated the detectable effect size (hazard ratios) for a change in a binary exposure variable (i.e., high physical activity vs. low, low TV viewing vs. high) at 80% power for each type of transition and separate for each type of disease model. To accomplish this, we specified the sample size, a two-sided test, an alpha of 0.05, 80% power, and the probability of failure for each type of transition (Tables 7 and 8).

For the CVD analysis and each type of transition, the hazard ratios necessary to detect a change at 80% power fall well within the range of published estimates for both physical activity and TV viewing with incident CVD and all-cause mortality. For the cancer analysis, the hazard ratios necessary to detect a minimal change for the health to disease and disease to death transition are stronger than that observed in most of the physical activity and TV viewing literature with incident cancer and survival after cancer diagnosis. For the cancer analysis, the range of hazard ratios for the health to death transition are within the range of published estimates for both the physical activity and sedentary behavior literature with all-cause mortality.

Table 7. Power analysis for CVD outcomes.

	Sample size	Number of events	Probability of failure	Hazard Ratio
Health to disease				
CHD	13,534	2426	0.18	0.89
Stroke	13,534	1144	0.08	0.84
HF	13,534	2602	0.19	0.90
Health to death				
CHD	13,534	4241	0.31	0.92
Stroke	13,534	4741	0.35	0.92
HF	13,534	3655	0.27	0.91
Disease to death				
CHD	2426	1234	0.51	0.85
Stroke	1144	734	0.64	0.81
HF	2602	1820	0.70	0.88

Probability of failure is calculated as number of events divided by sample size
Abbreviations: CHD= coronary heart disease, HF= heart failure

Table 8. Power analysis for cancer outcomes.

	Sample size	Number of events	Probability of failure	Hazard Ratio
Health to disease				
Colorectal	14508	361	0.025	0.75
Lung	14508	560	0.039	0.79
Prostate	6582	813	0.124	0.82
Breast	7849	564	0.072	0.79
Health to death				
Colorectal	14508	4870	0.336	0.92
Lung	14508	4572	0.315	0.92
Prostate	6582	2475	0.376	0.89
Breast	7849	2041	0.260	0.88
Disease to death				
Colorectal	361	184	0.510	0.66
Lung	560	482	0.861	0.77
Prostate	813	300	0.369	0.72
Breast	564	215	0.381	0.68

Probability of failure is calculated as number of events divided by sample size

CHAPTER 5: LEISURE-TIME PHYSICAL ACTIVITY AND TELEVISION VIEWING WITH LIFE EXPECTANCY FREE OF NONFATAL CARDIOVASCULAR DISEASE

5.1 Introduction

Cardiovascular disease (CVD) is the leading cause of death, premature mortality, and years lived with disability.[17] In the United States (US) over 92.1 million people have CVD (36.6%), about 16.5 million have been diagnosed with coronary heart disease (CHD), 7.2 million have had a stroke, and 6.5 million have been diagnosed with heart failure (HF).[30] This high burden of CVD suggests that many years of life may be spent living with CVD. It is therefore important to identify opportunities to extend the number of years lived free of CVD. Increasingly, studies have begun using health expectancy metrics that combine incidence and mortality to estimate years lived with and without disease.[18]

Greater amounts of physical activity have been associated with a reduced risk of CVD,[6, 115] all-cause mortality,[55, 115] a longer life expectancy,[55, 56] and, most recently, a longer CVD-free survival.[10-12] Results from observational studies suggest a positive association of physical activity with life expectancy free of CVD.[10-12] For example, in the Framingham cohort,[12] men who self-reported high levels of physical activity based on a weighted daily sum of activities could expect to live 22.8 years (95% confidence interval (CI) 21.6, 23.9) CVD-free, which was 3.2 years (95% CI 1.9, 4.3) more than men who self-reported low levels of physical activity (19.7 years CVD-free (95% CI 18.7, 20.6)). Research in this area has been limited to analysis of one population-based cohort in the US and three cohorts in Europe. Furthermore, existing studies

used various methods of physical activity ascertainment making it difficult to generalize findings to other populations.

Greater amounts of sedentary behavior are linked to an increased risk of incident CVD[9] and all-cause mortality.[60] Sedentary behavior, any waking behavior that expends little energy expenditure (≤ 1.5 metabolic equivalent of task (MET)) while in a sitting or reclining posture,[45] is highly prevalent, as on average, Americans spend about 8 hours per day in sedentary behaviors.[50] Little information exists on how sedentary behaviors are associated with years lived with and without CVD.

Our objective was to examine the associations between physical activity and sedentary behavior with life expectancy with and without disease for three types of CVD: CHD, stroke, and HF. Gaps in the existing literature addressed by this study include the assessment of physical activity as MET hours per week (MET-h/week) to account for intensity of activity and to enhance translation of results, and the inclusion of sedentary behavior for the first time.

5.2 Methods

5.2.1 Study population

We used data from the Atherosclerosis Risk in Communities (ARIC) Study. The ARIC Study is a population-based prospective cohort of 15,792 mostly white and African-American adults age 45 – 64 years at baseline. Participants were recruited from four geographic areas in the United States (Forsyth County, North Carolina; Jackson, Mississippi; Washington County, Maryland; and Minneapolis, Minnesota).[94] The study has conducted six examination visits (Visit 1 1987-89, Visit 2 1990-92, Visit 3 1993-95, Visit 4 1996-98, Visit 5 2011-13, and Visit 6 2016-17). Cohort members were asked to participate in interviews, clinical examinations, and annual (semi-annual since 2012) telephone interviews.[94] Participants provided written consent at each

examination. The ARIC study was approved by the Institutional Review Boards of the four participating ARIC Study centers.

5.2.2. Physical activity and sedentary behavior

Physical activity was ascertained at Visits 1 and 3 with the Baecke questionnaire.[102, 103] Participants were asked to list up to four leisure-time physical activities they participated in the past year and to provide the number of hours/week (duration) and months/year (frequency) for each activity. Activities were assigned a MET value based on the Compendium of Physical Activities.[104] Activities with a MET value of 3 or higher were classified as moderate-to-vigorous intensity.[38] The MET, frequency, and duration of each activity were used to calculate MET-h/week spent in leisure-time moderate-to-vigorous physical activity (LTPA). MET-h/week spent in LTPA at both visits was categorized as none, < median (0.1 – <13.2 MET-h/week), and ≥ median (13.2+ MET-h/week). The cut point was based on the Visit 1 median value of MET-h/week among those reporting any LTPA.

Television (TV) viewing, an indicator of sedentary behavior, was ascertained at Visit 1 with a question on how often participants viewed TV (response options included never, seldom, sometimes, often, and very often), which was further classified as never/seldom, sometimes, and often/very often due to small numbers in some categories.

5.2.3 All-cause mortality

Deaths were ascertained from cohort entry until December 31, 2016 and were identified by annual phone calls, active surveillance of hospitalizations in ARIC communities, and linkage with the National Death Index. Death certificates were reviewed by medical abstractors to determine underlying causes of death and the circumstances of death were confirmed with family members.[94, 95]

5.2.4. Cardiovascular disease outcomes

We separately examined incident nonfatal CHD, stroke, and HF. Prevalent CHD at baseline was defined as a myocardial infarction (MI) from Visit 1 ECG data, or a self-reported history of MI or coronary revascularization. Incident nonfatal CHD was defined as definite or probable MI, silent MI between examinations detected by electrocardiography, and cardiac revascularization procedures. MI events were identified from active surveillance of hospitalizations occurring among ARIC cohort members.[95, 96] Trained study personnel abstracted clinical information from the medical records of eligible hospitalizations. Definite or probable MI was defined from a diagnostic algorithm based on chest pain, electrocardiograms, and cardiac enzyme data.[95] A committee reviewed all CHD events and disagreements were adjudicated.

Prevalent stroke at baseline was defined as self-reported history of a stroke or transient ischemic attack. Incident nonfatal stroke events were identified by self-report from ARIC Visit examinations, annual follow-up telephone calls, and active surveillance of hospitalizations in the ARIC communities.[97] A trained nurse abstracted the medical record if a hospitalization had stroke diagnostic codes, if discharge summaries contained stroke related keywords, if neuroimaging had cerebrovascular findings, or if the patient had been admitted to the neurological intensive care unit.[97] Stroke events were classified as definite or probable by computer algorithm and a physician reviewer according to criteria adapted from the National Survey of Stroke.[97, 98] A second physician adjudicated disagreements.

Prevalent HF at baseline was defined as self-report of taking a medication for HF in the past two weeks or a score of three on the Gothenburg criteria.[99] Incident HF was identified by active surveillance of hospitalizations with ICD-9 code 428.xx in any position and relevant ICD-10 codes. Medical records of eligible hospitalizations that occurred after 2004 were abstracted

and independently reviewed by two trained and certified physicians on the ARIC HF Classification Committee.[100]

5.2.5. Covariates

Socio-demographic factors ascertained at Visit 1 and included in analyses were age, race by ARIC study field center (white Forsyth County, African American Forsyth County, white Washington County, white Minneapolis, African American Jackson), gender, and education (high school or less, vocational school, some college or college degree, higher than college degree).

Smoking status, alcohol intake, body mass index (BMI), blood pressure, diabetes, and high-density lipoprotein cholesterol (HDL-C) were assessed following a standardized protocol at all examination visits. Smoking status was based on self-report and categorized as never, former, and current smokers. Alcohol intake was measured by asking participants to report their usual intake of alcoholic beverages of a standard serving of wine, beer, and hard liquor per week. The alcohol amount of each type of drink (4 ounce glass of wine=10.8 grams (g), 12 ounces of beer=13.2g, and 1.5 ounce of hard liquor=15.1g) was multiplied by number of drinks and summed for a weekly intake. Alcohol intake was further categorized as no current intake, $\leq$ 100g, and > 100g.[105]

Weight and height were measured and used to calculate BMI as weight in kilograms (kg) divided by square of height in meters (m^2) (categorized as underweight/normal <25.0 kg/m^2, overweight 25.0 - < 30 kg/m^2, and obese $\geq$ 30.0 kg/m^2).[106] Seated blood pressure after 5 minutes of rest was measured at all visits by a trained technician. The average of the second and third measurement were used. Participants were classified as hypertensive if systolic blood pressure was $\geq$140 millimeters of mercury (mmHg), or diastolic blood pressure was $\geq$ 90mmHg, or

reported use of antihypertensive medication in the past two weeks. Diabetes status was considered positive if study participants had been told by a physician they had diabetes, or had a fasting plasma glucose ≥126 milligrams per deciliter (mg/dL), or had a non-fasting glucose ≥200 mg/dL, or reported use of hypoglycemic medication in the past two weeks. HDL-C was collected from 12 hour fasting blood samples drawn by venipuncture from an antecubital vein and specified as a continuous variable.

5.2.6. Statistical analysis

Of the 15,792 ARIC participants examined at baseline, we excluded participants with prevalent CVD (having prevalent CHD, stroke, or HF) (n=2,023), and participants who experienced a CVD event (CHD, stroke, or HF) or death within the first year of follow-up (n=132). Asian or American Indian/Alaskan Indian participants (n=48) and African American participants in Minnesota and Washington County (n=55) were excluded due to small numbers. After exclusions, the analytic set comprised 13,534 (86%) participants.

A non-recoverable illness-death multistate survival model was used to estimate how participants moved between health (state 1), disease (state 2), and all-cause mortality (state 3) states. In this model, participants started free of disease and moved: 1) from health to developing disease, or 2) from health to death from any cause. Once a participant developed disease, they could move from the disease state to all-cause mortality. Separate models were specified with different nonfatal disease states: CHD, stroke, and HF. No backward transitions were allowed between states. If a participant experienced a fatal disease event (date of CVD event and death were on the same day) they moved directly to the all-cause mortality state. In our analytic sample there were 282 fatal CHD events, 7 fatal stroke events, and 132 fatal HF events, in which these participants moved directly to the all-cause mortality state.

The multistate model was estimated as a Markov log-linear parametric model with an exponential distribution and time constant hazard using the msm R package.[108, 109] Hazard ratios (HR) and 95% confidence intervals (CI) were estimated for each type of transition. Time-varying covariates closest in time preceding each transition were used for the specific transition. Age was used as the time scale for models; participants started contributing time to the study at the age they entered at Visit 1. Follow-up continued until the date of last known contact with each participant, death, or end of study (December 31, 2016).

Life expectancy at age 50 (upper limit 95 years), the expected average number of remaining years of life in health and disease states conditional on reaching age 50, was calculated using the Estimating Life Expectancies in Continuous Time (ELECT) R package.[110] We estimated life expectancies at age 50 by level of LTPA and TV by examining these factors separately in models and then specified models that included both LTPA and TV. All models were adjusted for age, gender, race by ARIC center, education, smoking, and alcohol intake. In LTPA models that did not include TV, we also evaluated the impact of additional adjustment for BMI, diabetes status (yes, no), hypertension (yes, no), and HDL-C (continuous) in addition to previously mentioned confounders. The additional covariates were limited to sensitivity analyses because they could mediate transitions between LTPA from health to disease, health to all-cause mortality, and disease to all-cause mortality.

We used Multiple Imputation by Chained Equations (MICE) to impute missing exposure and covariate data that occurred at each visit.[111, 112] We imputed 10 datasets and the multistate models and life expectancies were estimated in each imputed data set. The hazard ratios, standard errors, and life expectancy estimates were averaged using Rubin's rule.[113] All analyses

were carried out with SAS Version 9.4 (Cary, North Carolina) and R Version 3.3.2 and approved by the Institutional Review Board of University of North Carolina at Chapel Hill.

5.3 Results

The average age at Visit 1 was 54 years (SD 5.7 years), 56% of participants were female, 26% African American, and 55% had received a high school education or less (Table 9). At Visit 1, almost 40% reported no LTPA; of those who reported LTPA the median was 13.2 MET hours per week. Close to half of all participants viewed TV sometimes (47%).

Over a median of 27.2 years of follow-up, 4,519 (34%) participants experienced at least one nonfatal CVD event and 5,475 (40%) died. The average age at incident nonfatal CHD was 69 years (SD 8.5), 72 years (SD 8.6) at incident nonfatal stroke, and 74 years (SD 8.5) at incident nonfatal HF.

5.3.1 LTPA and TV viewing with nonfatal CVD and death

Engagement in any level of LTPA compared to none was associated with a reduced risk of developing nonfatal CHD, stroke, and HF (Table 10). Participation in any LTPA compared to none was also associated with a lower risk of all-cause mortality in the absence of having each type of CVD. Participants who engaged in LTPA $\geq$ median compared to none had a lower risk of all-cause mortality after developing nonfatal CHD. Similarly, for nonfatal HF, engagement in any level of LTPA compared to none was associated with lower risk of all-cause mortality after developing nonfatal HF. Results were not sensitive to controlling for additional factors (BMI, hypertension, diabetes, HDL-C) that may act as mediators or confounders.

Watching TV seldom/never compared to viewing TV often/very often was associated with a reduced risk of nonfatal CHD and HF, but was not associated with nonfatal stroke (Table 11). Across all diseases, watching TV sometimes or seldom/never was associated with a lower

risk of all-cause mortality in the absence of having each type of CVD. The associations of TV viewing with all-cause mortality after developing each disease were close to the null.

The hazard ratios from models that included both LTPA and TV were similar to the models that separately examined these factors.

5.3.2 LTPA with nonfatal CHD, stroke, and HF life expectancy

Engagement in any LTPA compared to none was associated in a positive dose response fashion with a longer nonfatal disease-free life expectancy for each type of CVD (Figure 6). At LTPA levels < median, life expectancy disease-free was ~ 0.8 years longer compared to no LTPA for each type of nonfatal CVD. At LTPA $\geq$ median, compared to no LTPA, disease-free life expectancy was ~1.5 years longer (CHD: men 1.5 years (95% CI 1.0, 2.0), women 1.6 years (95% CI 1.1, 2.2), stroke: men 1.8 years (95% CI 1.2, 2.3), women 1.8 years (95% CI 1.3, 2.3), HF: men 1.6 years (95% CI 1.1, 2.1), women 1.7 years (95% CI 1.2, 2.2)). For each type of CVD, life expectancy with disease was similar for three levels of LTPA.

5.3.3 TV with nonfatal CHD, stroke, and HF life expectancy

Watching TV sometimes or seldom/never was associated with longer disease-free life expectancy compared to often/very often viewing (Figure 7). For example, compared to participants who often/very often viewed TV, participants who seldom/never watched had a longer nonfatal CHD-free life expectancy (men 1.1 years (95% CI 0.5, 1.7), women 0.9 years (95% CI 0.3, 1.6)), greater nonfatal stroke-free life expectancy (men 0.8 years (95% CI 0.2, 1.4), women 0.8 years (95% CI 0.2, 1.4)), and greater nonfatal HF-free life expectancy (men 0.9 years (95% CI 0.3, 1.5), women 1.0 years (95% CI 0.4, 1.6)). Across all diseases, the life expectancy disease-free was similar for the sometimes and seldom/never viewing TV levels. For each type of CVD, the life expectancy with nonfatal disease was similar by level of TV viewing.

5.3.4 Models with both LTPA and TV with nonfatal CHD, stroke, and HF life expectancy

Across all diseases, participants who engaged in LTPA ≥ median and seldom/never viewing TV had ~2.5 year greater nonfatal disease-free life expectancy compared to participants who reported no LTPA and often/very often watching TV (Figure 8) (CHD: men 2.4 years (95% CI 1.7, 3.2), women 2.4 years (95% CI 1.7, 3.2); stroke: men 2.4 years (95% CI 1.6, 3.1), women 2.4 years (95% CI 1.7, 3.2), HF: men 2.4 years (95% CI 1.7, 3.1), women 2.5 years (95% CI 1.8, 3.2)).

5.4 Discussion

In this large prospective cohort of adults, engagement in any level of LTPA was associated with longer nonfatal CVD-free life expectancy when compared to engaging in no LTPA. Such associations were observed for nonfatal CHD, stroke, and HF. The inverse association of TV viewing with CVD-free life expectancy outcomes was of modest magnitude, with a small gain in CVD-free life expectancy for viewing TV sometimes and seldom/never compared to often/very often TV viewing.

The observed pattern of an extended disease-free life expectancy with higher LTPA levels is consistent with published reports.[10-12] In reports from the Framingham cohort, participants who self-reported high as compared to low levels of physical activity, had CVD-free life expectancy that was longer by about three years.[11, 12] However, it is difficult to compare our MET-h/week of LTPA with the physical activity measurement used in the Framingham cohort, which was estimated as a weighted sum of daily activities based on sleeping, resting, and engaging in light, moderate, or heavy activity.[12] O'Doherty et al.[10] separately analyzed data from three European-based cohorts and observed that participation in vigorous activity compared to no vigorous physical activity was associated with a longer CVD-free life expectancy

(estimates ranged from three to five years). Although we found similar trends in LTPA extending years spent free of CVD, the magnitude of our findings was smaller compared to these other studies. These differences may be due to characteristics of each cohort, the various methods of physical activity measurement, and different analytic methods and covariates used.

Our report extends the understanding of how physical activity is associated with CVD life expectancy outcomes by measuring LTPA as MET-h/week to account for intensity of activity and separately examining three types of CVD. We observed a positive dose-response relationship between LTPA and nonfatal disease-free life expectancy. At LTPA < median, nonfatal disease-free life expectancy was longer by more than half a year for each type of CVD compared to no LTPA. At LTPA $\geq$ median, we observed close to two years longer nonfatal disease-free life expectancy compared to no LTPA. For reference, a person who engages in a walk at 3 miles per hour, estimated to be 3.3 METs, for five days of the week, at 50 minutes per day can expend 13.8 MET-h/week.

We separately examined three types of nonfatal CVD and observed homogeneity of associations of LTPA with nonfatal CHD, stroke, and HF. The hazard ratios we estimated for how LTPA was associated with nonfatal incident CHD, stroke, and HF are consistent with existing research in regards to the direction and magnitude of estimates when physical activity has been specified as MET-h/week.[6] The similarities of associations of LTPA with these three CVDs may be because physical activity has been linked to reduced adiposity, improved blood pressure, prevention of diabetes, and improvement in lipid profiles, factors that are all risk factors for CHD, stroke, and HF.[31]

Our study is the first, to our knowledge, to examine how sedentary behavior is associated with nonfatal CVD life expectancy outcomes. We observed a gain in nonfatal disease-free life

expectancy of approximately one year for sometimes and seldom/never viewing TV compared to often/very often viewers, but the estimates for the sometimes and seldom/never TV viewers were similar with overlapping confidence intervals. Our associations of hazard ratios of TV viewing with incident nonfatal CVD and all-cause mortality are in the same direction as existing literature but are somewhat weaker.[61, 62] Often TV viewing is measured as hours per week spent viewing and studies using this type of measure have estimated a higher risk of incident CVD at two hours of viewing per day or higher, and a higher risk of all-cause mortality at three and four hours per day of viewing.[61, 62] A limitation of our study is that it did not assess the number of hours spent watching TV.

We analyzed each type of nonfatal CVD separately, but observed that 32% participants who developed CVD did experience multiple CVD events. In additional analysis we estimated life expectancy at age 50 for a composite CVD outcome that was the first occurrence of nonfatal CHD, stroke, or HF. The life expectancy differences by LTPA and TV with the composite CVD outcome were similar to associations observed when examining each disease individually. However, nonfatal life expectancy CVD-free was lower and life expectancy with nonfatal CVD was higher than the respective life expectancy estimates when separately examining each disease.

To estimate life expectancy CVD-free we used a health expectancy outcome, a summary measure that estimates expected years to live in good and poor health. Improving and maintaining the health of older adults is a priority, as this population is projected to grow and chronic diseases often develop at older ages.[13] Other strengths of this study include use of time-varying covariates, well-measured outcomes from active surveillance and adjudication of outcomes, long-term follow-up of over 30 years, and multiple imputation of exposure and

covariate data. Although we included time-varying measurements of physical activity, we did not have a physical activity measurement after Visit 3 and we used a baseline measure of TV viewing. It is possible participant levels for both types of behaviors changed after the last measurement of each.

Limitations of this report include the self-reported nature of LTPA and extent of TV viewing, and having a single domain of physical activity and sedentary behavior. Levels of physical activity tend to be overestimated when collected by self-report; however, the Baecke questionnaire is similar in reliability and validity to other physical activity questionnaires.[116, 117] We included physical activity during leisure-time and did not include activity that takes place during occupation, transport, or housework activities. It is possible our associations could be stronger with the inclusion of physical activity that occurs from multiple domains. TV viewing represents only one domain of sedentary behavior and does not include time spent sitting for work or transport.

5.5. Conclusion

Engagement in any level of LTPA and viewing TV sometimes or seldom/never were associated with longer life expectancy free of nonfatal CHD, stroke, and HF. Our findings suggest that engaging in LTPA and watching less TV could increase the number of years lived free of nonfatal CHD, stroke, and HF.

Table 9. Visit 1 characteristics of ARIC Study participants by LTPA and TV viewing (n=13,534).

	Leisure-time physical activity			TV viewing			Overall
	None	< median	≥ median	Seldom/ never	Sometimes	Often/ very often	
	N=5114	N=4207	N=4207	N=2601	N=6393	N=4528	N=13,534
Age at V1, mean(SD)	54.3 (5.7)	54.4 (5.7)	54.5 (5.8)	53.9 (5.7)	54.4 (5.7)	54.7 (5.8)	54.4 (5.7)
Male, %	2045 (40.0)	1643 (39.1)	2222 (52.8)	1027 (39.5)	2650 (41.5)	2231 (49.3)	5915 (43.7)
ARIC center, n(%)							
Forsyth County	1111 (21.7)	1148 (27.3)	1225 (29.1)	694 (26.7)	1681 (26.3)	1107 (24.5)	3485 (25.8)
Jackson	1893 (37.0)	722 (17.2)	552 (13.1)	370 (14.2)	1484 (23.2)	1313 (29.0)	3171 (23.4)
Minneapolis	915 (17.9)	1255 (29.8)	1406 (33.4)	866 (33.3)	1636 (25.6)	1074 (23.7)	3576 (26.4)
Washington County	1195 (23.4)	1082 (25.7)	1024 (24.3)	671 (25.8)	1592 (24.9)	1034 (22.8)	3302 (24.4)
White race/ethnicity, n(%)	3076 (60.2)	3333 (79.2)	3566 (84.8)	2190 (84.2)	4773 (74.7)	3006 (66.4)	9977 (73.7)
African American race/ethnicity, n(%)	2038 (39.9)	874 (20.8)	641 (15.2)	411 (15.8)	1620 (25.3)	1522 (33.6)	3557 (26.3)
Education, n(%)							
high school or less	3355 (65.7)	2234 (53.2)	1808 (43.0)	1230 (47.3)	3436 (53.8)	2726 (60.3)	7403 (54.8)
vocational	386 (7.6)	387 (9.2)	365 (8.7)	208 (8.0)	551 (8.6)	378 (8.4)	1138 (8.4)
college	987 (19.3)	1168 (27.8)	1398 (33.3)	821 (31.6)	1702 (26.7)	1030 (22.8)	3553 (26.3)
graduate/professional	376 (7.4)	414 (9.9)	632 (15.0)	339 (13.1)	695 (10.9)	388 (8.6)	1422 (10.5)
Missing	10	4	4	3	9	6	18
Leisure-time physical activity, n(%)							
no LTPA				807 (31.0)	2408 (37.7)	1897 (41.9)	5114 (37.8)
< median				791 (30.4)	1941 (30.4)	1473 (32.5)	4207 (31.1)
≥ median				1003 (38.6)	2044 (32.0)	1158 (25.6)	4207 (31.1)
Missing				0	0	0	6
TV viewing, n(%)							
seldom/never	807 (15.8)	791 (18.8)	1003 (23.9)				2601 (19.2)
sometimes	2408 (47.1)	1941 (46.2)	2044 (48.6)				6393 (47.3)
often/very often	1897 (37.1)	1473 (35.0)	1158 (27.5)				4528 (33.5)
Missing	2	2	2				12
Smoking, n(%)							
current smoker	1616 (31.6)	994 (23.6)	833 (19.8)	521 (20.1)	1540 (24.1)	1381 (30.5)	3446 (25.5)
past smoker	1347 (26.4)	1311 (31.2)	1584 (37.7)	836 (32.2)	1971 (30.8)	1435 (31.7)	4244 (31.4)
never smoker	2147 (42.0)	1900 (45.2)	1788 (42.5)	1242 (47.8)	2880 (45.1)	1708 (37.8)	5836 (43.2)
Missing	4	2	2	2	2	4	8
Alcohol intake, n(%)							
not current drinker	3419 (67.4)	2543 (60.7)	2185 (52.2)	1586 (61.2)	3886 (61.1)	2669 (59.3)	8150 (60.5)
≤ 100 grams	1020 (20.1)	1114 (26.6)	1303 (31.1)	671 (25.9)	1635 (25.7)	1131 (25.1)	3437 (25.5)

	Leisure-time physical activity			TV viewing			Overall
	None	< median	≥ median	Seldom/ never	Sometimes	Often/ very often	
	N=5114	N=4207	N=4207	N=2601	N=6393	N=4528	N=13,534
> 100 grams	637 (12.6)	535 (12.8)	701 (16.7)	333 (12.9)	842 (13.2)	698 (15.5)	1875 (13.9)
Missing	38	15	18	11	30	30	72
BMI, mean (SD)	28.5 (5.8)	27.2 (5.0)	26.7 (4.5)	26.7 (4.9)	27.5 (5.2)	28.0 (5.4)	27.5 (5.2)
Missing	5	2	1	2	1	5	8
Have hypertension, n(%)	1917 (37.5)	1230 (29.3)	1087 (25.9)	652 (25.1)	1971 (30.9)	1611 (35.6)	4237 (31.3)
Missing	7	5	2	0	9	4	14
Have diabetes, n(%)	649 (12.9)	395 (9.4)	332 (7.9)	202 (7.8)	631 (10.0)	542 (12.1)	1377 (10.3)
Missing	64	20	24	14	52	42	108
HDL-C, mean(SD)	51.8 (17.0)	52.6 (16.7)	52.6 (17.3)	54.4 (17.6)	52.5 (16.7)	50.9 (17.0)	52.3 (17.0)
Missing	119	39	31	23	94	72	189

Abbreviations: BMI= body mass index, HDL-C high density lipoprotein cholesterol, LTPA= leisure-time moderate-to-vigorous physical activity, MET= metabolic equivalent of task

LTPA categories: < median (0.1 - < 13.2 MET-h/week), ≥ median (13.2+ MET-h/week)

Table 10. Associations (hazard ratios (95% CI)) of LTPA with nonfatal CHD, stroke, HF, and all-cause mortality, ARIC participants (n=13,534).

	health to disease	health to death HR (95% CI)	disease to death
Nonfatal CHD			
Number of events	2,426	4,241	1,234
Sum of person-years	292,957	292,957	23,887
LTPA			
No LTPA	ref	ref	ref
< median	0.92(0.82,1.02)	0.91(0.84,0.99)	0.98(0.84,1.13)
≥ median	0.88(0.79,0.97)	0.80(0.74,0.87)	0.83(0.72,0.96)
Nonfatal Stroke			
Number of events	1,144	4,741	734
Sum of person-years	309,746	309,746	7,099
LTPA			
No LTPA	ref	ref	ref
< median	0.86(0.74,1.00)	0.92(0.85,0.99)	1.06(0.88,1.28)
≥ median	0.80(0.68,0.92)	0.80(0.74,0.86)	1.01(0.83,1.23)
Nonfatal HF			
Number of events	2,602	3,655	1,820
Sum of person-years	304,313	304,313	12,531
LTPA			
No LTPA	ref	ref	ref
< median	0.87(0.79,0.95)	0.94(0.87,1.02)	0.88(0.79,0.99)
≥ median	0.80(0.72,0.88)	0.82(0.76,0.89)	0.82(0.73,0.92)

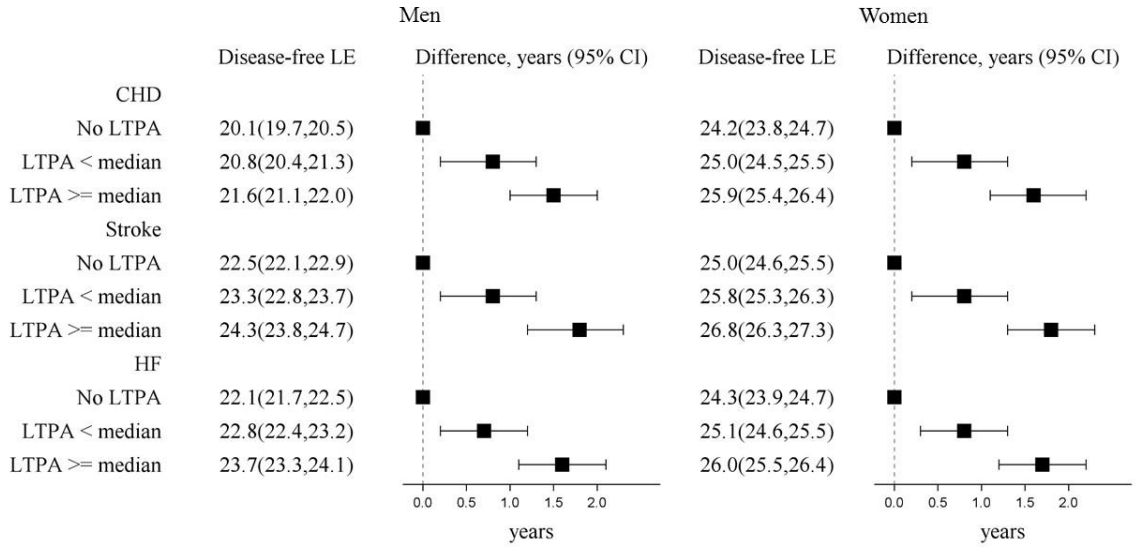
LTPA categories: < median (0.1 - < 13.2 MET-h/week), ≥ median (13.2+ MET-h/week)
Models specified separately for each type of disease state. Models adjusted for age, gender, race by ARIC center, education, smoking, and alcohol intake. Abbreviations: CI= confidence interval, CHD= coronary heart disease, HF= heart failure, HR= hazard ratio, LTPA=leisure-time moderate-to-vigorous physical activity, MET= metabolic equivalent of task

Table 11. Associations (hazard ratio (95% CI)) of TV viewing with nonfatal CHD, stroke, HF, and all-cause mortality, ARIC participants (n=13,534).

	health to disease	health to death HR (95% CI)	disease to death
Nonfatal CHD			
Number of events	2,426	4,241	1,234
Sum of person-years	292,957	292,957	23,887
TV viewing			
Often/very often	ref	ref	ref
Sometimes	0.98(0.89,1.07)	0.92(0.86,0.99)	0.89(0.79,1.01)
Seldom/never	0.83(0.74,0.94)	0.91(0.84,1.00)	0.93(0.79,1.11)
Nonfatal Stroke			
Number of events	1,144	4,741	734
Sum of person-years	309,746	309,746	7,099
TV viewing			
Often/very often	ref	ref	ref
Sometimes	0.98(0.86,1.12)	0.90(0.85,0.96)	1.04(0.89,1.22)
Seldom/never	0.98(0.82,1.17)	0.89(0.82,0.97)	0.95(0.76,1.19)
Nonfatal HF			
Number of events	2,602	3,655	1,820
Sum of person-years	304,313	304,313	12,531
TV viewing			
Often/very often	ref	ref	ref
Sometimes	0.81(0.74,0.88)	0.97(0.90,1.04)	0.97(0.87,1.07)
Seldom/never	0.87(0.78,0.97)	0.91(0.82,1.00)	1.02(0.89,1.17)

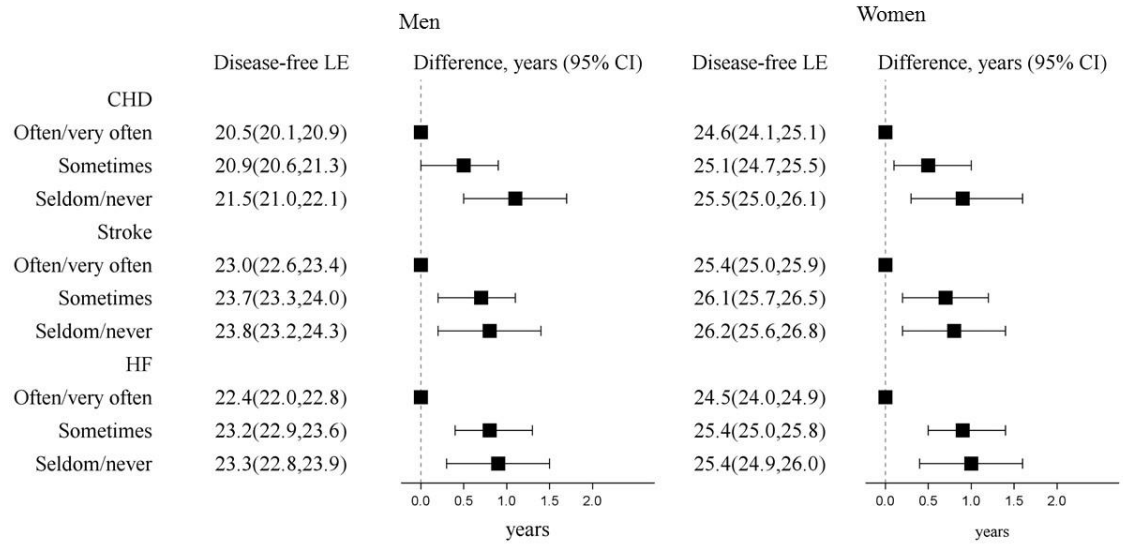
Models specified separately for each type of disease state. Models adjusted for age, gender, race by ARIC center, education, smoking, and alcohol intake. Abbreviations: CI= confidence interval, CHD= coronary heart disease, HF= heart failure, HR= hazard ratio

Figure 6. Life expectancy (years) free of nonfatal cardiovascular disease and life expectancy differences at age 50 by LTPA, ARIC participants (n=13,534).



LTPA categories: < median (0.1 - < 13.2 MET-h/week), ≥ median (13.2+ MET-h/week)
All disease states are nonfatal. Models specified separately for each type of disease state. Models adjusted for age, gender, race by ARIC center, education, smoking status, and alcohol intake. Abbreviations: CHD= coronary heart disease, CI = confidence interval, HF= heart failure, LE= life expectancy, LTPA=leisure-time moderate-to-vigorous physical activity, MET= metabolic equivalent of task

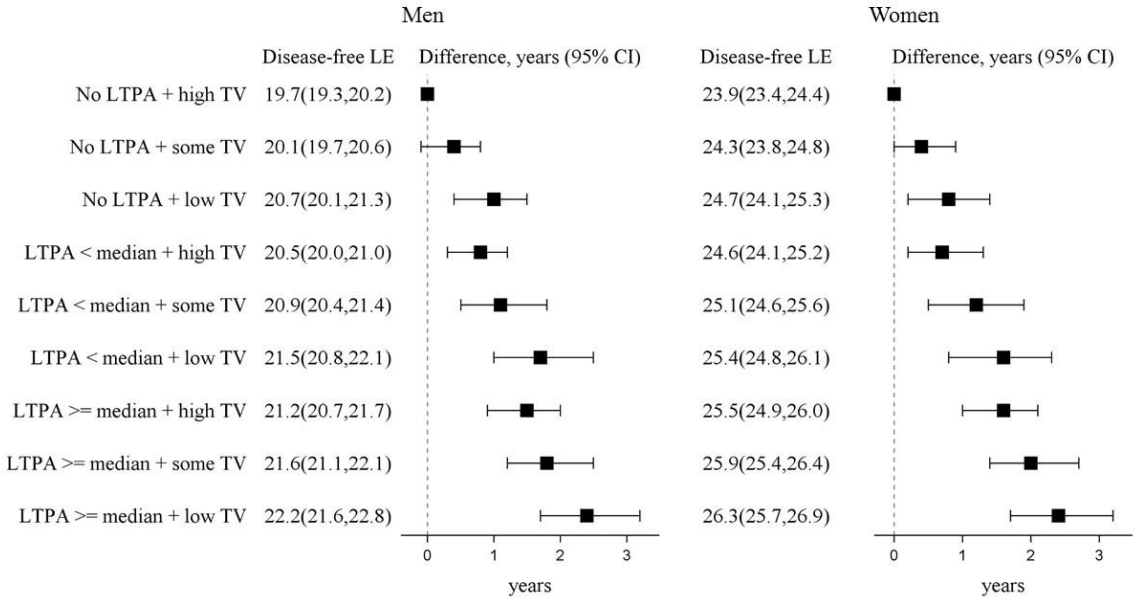
Figure 7. Life expectancy (years) free of nonfatal cardiovascular disease and life expectancy differences at age 50 by TV viewing, ARIC participants (n=13,534).



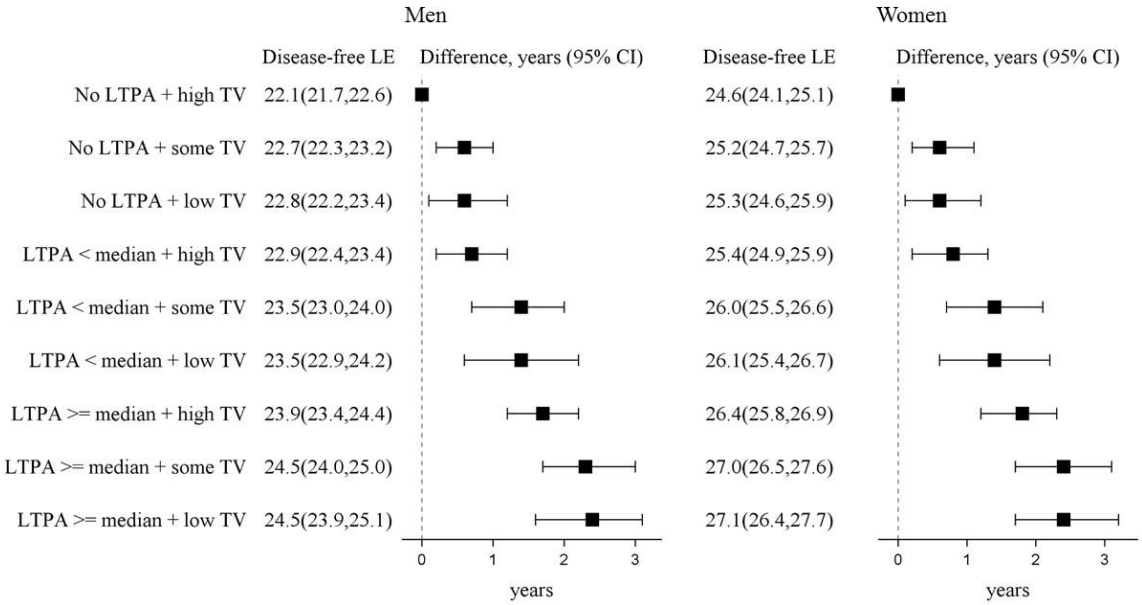
All disease states are nonfatal. Models specified separately for each type of disease state. Models adjusted for age, gender, race by ARIC center, education, smoking status, and alcohol intake. Abbreviations: CHD = coronary heart disease, CI = confidence interval, HF= heart failure, LE= life expectancy

Figure 8. Life expectancy (years) free of nonfatal cardiovascular disease and life expectancy differences at age 50 by LTPA and TV viewing, ARIC participants (n=13,534).

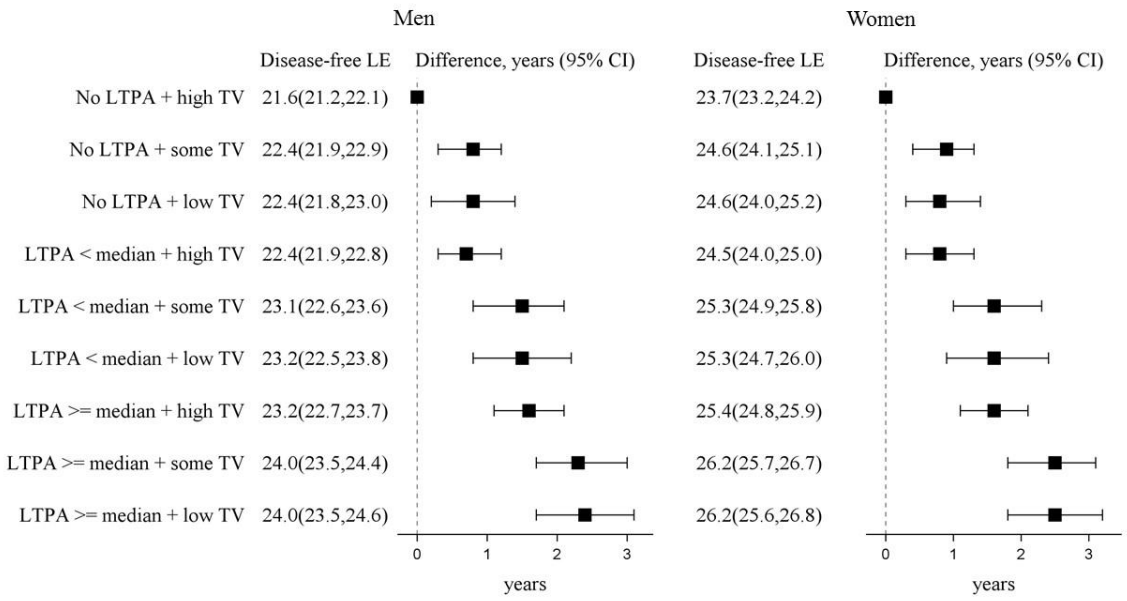
a) nonfatal CHD



b) nonfatal Stroke



3c) nonfatal HF



LTPA categories: < median (0.1 - < 13.2 MET-h/week), ≥ median (13.2+ MET-h/week)
TV categories: high TV is viewing often/very often, some TV is sometimes viewing, and low TV is seldom/never viewing TV. Models specified separately for each type of disease state. Models adjusted for age, gender, race by ARIC center, education, smoking status, and alcohol intake. Abbreviations: CI = confidence interval, LE= life expectancy, LTPA=leisure-time moderate-to-vigorous physical activity, MET= metabolic equivalent of task.

CHAPTER 6: LEISURE-TIME PHYSICAL ACTIVITY AND TELEVISION VIEWING WITH LIFE EXPECTANCY FREE OF CANCER

6.1 Introduction

Cancer contributes significantly to years lived with disability and to the risk of mortality.[118] In the United States (US), 15.5 million men and women have a personal cancer history[32] and by 2020 this number is expected to increase to 18 million.[119] Prostate, breast, lung and bronchus, and colorectal cancer account for 46% of newly diagnosed invasive cancers among men and women.[32] The number of years lived without cancer can be estimated with health expectancy outcomes, a measure that combines incidence and mortality to divide life expectancy into life expectancy with and without disease.[18]

Physical activity has been associated with a reduced risk of many types of cancer,[7] longer survival after cancer diagnosis,[120] and longer life expectancy.[55] Recent studies on physical activity and health expectancy outcomes have observed that greater amounts of physical activity were associated with longer disease-free life expectancy from cardiovascular disease (CVD),[10, 12] diabetes,[25] and chronic disease (a composite measure of CVD, diabetes, and cancer)[28] but no studies have separately examined specific cancer types. Sedentary behavior, conversely, has been associated with an increased risk of incident cancer[8] and all-cause mortality.[60] To date, sedentary behavior has not been examined in relation to cancer health expectancy outcomes.

We sought to understand how physical activity and sedentary behavior were associated with cancer health expectancy outcomes, with particular focus on life expectancy cancer-free. Therefore, we examined how physical activity and television (TV) viewing, a common type of

sedentary behavior, were associated with life expectancy free of four leading types of cancer - colorectal, lung, prostate, and postmenopausal breast cancer, in a population-based cohort of adults from the Atherosclerosis Risk in Communities (ARIC) Study.

6.2 Methods

6.2.1 Study population

We used data from the ARIC Study, a prospective cohort of 15,792 mostly white and African-American adults. Participants, age 45 – 64 years at Visit 1, were enrolled from four geographic areas in the US (Forsyth County, North Carolina; Jackson, Mississippi; Washington County, Maryland; and Minneapolis, Minnesota). Six examination visits have been conducted (Visit 1 1987-89, Visit 2 1990-92, Visit 3 1993-95, Visit 4 1996-98, Visit 5 2011-13, and Visit 6 2016-17). Cohort members were asked to participate in interviews, clinical examinations, and annual (semi-annual from 2012) telephone follow-up interviews.[94] All participants provided informed consent at each study visit. The ARIC study was approved by the Institutional Review Boards of the four participating ARIC Study centers.

6.2.2 Physical activity and sedentary behavior

At Visits 1 and 3 participants were asked to complete the Baecke questionnaire and list up to four leisure-time physical activities they participated in during the past year.[102, 103] For each activity, the number of hours/week (duration) and months/year (frequency) were reported and a metabolic equivalent of task (MET) value was assigned based on the Compendium of Physical Activities.[104] Activities with a MET value of 3 or higher were classified as moderate to vigorous intensity.[38] The MET, frequency, and duration of each activity were used to calculate MET hours per week (MET-h/week) spent in leisure-time moderate-to-vigorous physical activity (LTPA). MET-h/week spent in LTPA at Visits 1 and 3 was categorized as none, < median (0.1 –

<13.2 MET-h/week), and ≥ median (13.2+ MET-h/week). The cut point was based on the Visit 1 median value of MET-h/week among those reporting any LTPA.

Sedentary behavior, any waking behavior that expends little energy expenditure (≤ 1.5 MET) while in a sitting or reclining posture,[45] was assessed with a question on TV viewing. Participants were asked at Visit 1 how often they viewed TV (never, seldom, sometimes, often, very often) and classified as never/seldom, sometimes, and often/very often due to small numbers in some categories.

6.2.3 Cancer and all-cause mortality outcomes

First primary invasive cancer diagnoses (postmenopausal breast, prostate, lung, and colorectal) were ascertained by linkage with statewide cancer registries from 1987 through December 31, 2012.[101] Some of the state cancer registries were not complete or established at the start of the ARIC study, and for this time period, cancer cases were identified by surveillance of hospital discharge summaries in the ARIC Study regions and confirmed with medical record abstraction.[101] The ARIC Cancer Coordinating Center adjudication teams adjudicated all potential cancer cases.[101] Participants were considered to have prevalent cancer at Visit 1 if a doctor had told them that they had cancer.

Deaths were ascertained from Visit 1 until December 31, 2012 through active surveillance of vital status and by linkage with the National Death Index. Medical records were abstracted and circumstances of the death confirmed with family members.[94, 95]

6.2.4 Covariate assessment

We included the following socio-demographic factors as covariates: age (continuous), race by ARIC center (white Forsyth County, African American Forsyth County, white

Washington County, white Minneapolis, African American Jackson), gender, and education (≤high school, vocational school, some college/college degree, graduate/professional).

Time updated covariates collected at all examination visits were smoking status (never, former, current smoker), alcohol intake, body mass index (BMI), and use of menopausal hormone therapy (MHT). Alcohol intake (no current intake, ≤ 100g, > 100g)[105] was obtained by asking participants to report their usual intake of alcoholic beverages of a standard serving of wine, beer, and hard liquor per week. Weekly alcohol intake was derived as the sum of the alcohol amount of each type of drink (4 ounce glass of wine=10.8 grams (g), 12 ounces of beer=13.2g, 1.5 ounce of hard liquor=15.1g) multiplied by the number of drinks. BMI (weight in kilograms (kg) divided by square of height in meters (m^2)) was calculated from interviewer measured weight and height and participants were classified according to standard BMI categories (underweight/normal <25.0 kg/m^2, overweight 25.0 - < 30 kg/m^2, obese ≥ 30.0 kg/m^2).[106] At each visit women self-reported use of MHT (never users, former users of any MHT type, current users of unopposed estrogen, current users of estrogen plus progestin).

Food consumption was collected at Visit 1 with a modified version of a 66-item food frequency questionnaire.[107] Daily servings of red meat intake was derived based on how often participants reported consuming hamburgers, hot dogs, processed meats, bacon, and beef, pork, or lamb in the past year.

Women were considered postmenopausal at the ARIC Visit in which they reported the following: 1) having both ovaries removed, or 2) if both ovaries had not been removed, they were not taking hormones and had not had a hysterectomy, then they were considered menopausal when they reported reaching menopause or having no periods in the past two years, or 3) if both ovaries had not been removed but women reported taking hormones, or had a

hysterectomy, or did not know their menopause status, then they were considered menopausal when they reached the average cohort race- and smoking status- specific age when menopause was reached (White- Never: 48.3, Former: 47.3 Current: 46.6; African American- Never: 47.8, Former: 47.0, Current: 45.6).

6.2.5 Statistical analysis

Of the 15,792 ARIC participants examined at baseline, we excluded participants who did not consent to non-cardiovascular disease research (n=149) and those with prevalent cancer at baseline (n=902). We excluded participants who experienced cancer (colorectal, lung, prostate, or breast) or death within the first year of follow-up (n=130) to establish temporality between physical activity and TV viewing with cancer and mortality outcomes. We also excluded Asian and American Indian/Alaskan Indian participants (n=48) and African American participants in Minnesota and Washington County (n=55) due to small numbers at these sites. After exclusions, 14,508 (92%) participants were included in analysis for colorectal and lung models, 6,582 men for prostate models and 7,849 women for postmenopausal breast models (77 women were not included in breast cancer models because they died or developed breast cancer before reaching menopause).

We used multistate survival models to estimate how participants moved between health (state 1), disease (state 2), and all-cause mortality (state 3) states. This model had three possible transitions – health to disease, health to all-cause mortality, and disease to all-cause mortality. Each type of cancer was the disease state in separate models. For each type of transition, hazard ratios (HR) and 95% confidence intervals (CI) were estimated with the msm R package.[108, 109] The time scale for all models was age; participants started contributing time to the study at the age they entered at Visit 1. For breast cancer analyses, women started contributing time at the

age of the visit in which they were considered postmenopausal. Follow-up continued until death or end of study (December 31, 2012). Time-varying covariates closest in time preceding each type of transition were used for the specific transition.

We estimated life expectancy at age 50 with the Estimating Life Expectancies in Continuous Time (ELECT) R package separately for men and women.[110] Life expectancy was defined as the expected average number of remaining years of life in health and disease states conditional on reaching age 50 and regardless of health status at age 50. We estimated life expectancy by level of LTPA and TV viewing. First we specified models that separately examined LTPA and TV and then specified models that included both LTPA and TV. For all models, confounders included age, gender, race by ARIC center, education, smoking, and alcohol intake.

We examined if results were sensitive to adjustment for BMI by adding it as a covariate to the models in which LTPA and TV were separately examined. Further sensitivity analyses included adding MHT to the breast cancer LTPA model and daily servings of red meat to the colorectal LTPA model, both potential cancer-specific confounders.

Missing exposure and covariate data that occurred at each visit were imputed with Multiple Imputation by Chained Equations (MICE).[111, 112] We imputed 10 datasets and the hazard ratios, standard errors, and life expectancy estimates from each dataset were averaged using Rubin's rule.[113] All analyses were carried out with SAS Version 9.4 (Cary, North Carolina) and R Version 3.3.2. Analyses were approved by the Institutional Review Board at the University of North Carolina at Chapel Hill.

6.3 Results

At baseline, the average age of participants was 54 years (SD 5.7), 55% were female, 28% were African American, 56% had a high school education or less, and most participants were not current smokers or current drinkers (Table 12). Over 60% of participants reported any LTPA and 47% reported watching TV sometimes. Ninety percent of women were postmenopausal at Visit 1 and the average daily red meat intake was 1.1 servings.

Over a median 23.6 years of follow-up, 2,360 (16.3%) participants had a diagnosis of incident invasive first primary colorectal, lung, prostate, or postmenopausal breast cancer and 5,054 (34.8%) deaths occurred in the full cohort. The average age at cancer diagnosis was 68.8 years (SD 7.5) for colorectal, 69.7 years (SD 7.3) for lung, 68.6 years (SD 6.3) for prostate, and 66.7 years (SD 7.3) for postmenopausal breast cancer.

6.3.1 LTPA and TV viewing with cancer and all-cause mortality

Compared to no LTPA, engagement in any LTPA was associated with a lower risk of lung cancer, and at LTPA $\geq$ median, a lower risk of colorectal and breast cancer (Table 13). Across all models, engagement in LTPA showed an inverse dose-response relationship with all-cause mortality in the absence of cancer. Participants who engaged in any level of LTPA had a lower risk of all-cause mortality following a breast cancer diagnosis. In sensitivity analysis, we added BMI to these models and observed similar hazard ratios. Results were similarly robust to the addition of MHT to the breast cancer model and daily red meat servings to the colorectal cancer model.

Level of TV viewing was not associated with incidence of cancer, of any type (Table 14). Watching TV sometimes or seldom/never compared to often/very often was associated with a lower risk of all-cause mortality in the absence of cancer. TV viewing was not associated with

all-cause mortality after developing cancer. We added BMI to these models and observed similar hazard ratios.

In models that mutually adjusted for both LTPA and TV, the hazard ratios were similar to when LTPA and TV were separately examined.

6.3.2 LTPA with colorectal, lung, prostate, and postmenopausal breast cancer life expectancy

For each cancer type, engagement in LTPA showed a positive dose-response relationship with greater cancer-free life expectancy. For example, for colorectal, lung, and breast cancer, participants who engaged in LTPA < median had ~1 year greater cancer-free life expectancy compared to participants who reported no LTPA. At LTPA ≥ median compared to none, participants had a greater cancer-free life expectancy of over 2 years for colorectal (men 2.2 years (95% CI 1.7, 2.7), women 2.3 years (95% CI 1.7, 2.8)), lung (men 2.1 years (95% CI 1.5, 2.6), women 2.1 years (95% CI 1.6, 2.7)), and breast cancer (2.4 years (95% CI 1.4, 3.3)), and over 1 year for prostate cancer (1.5 years (95% CI 0.8, 2.2)) (Figure 9). Life expectancy with cancer was similar by level of LTPA for colorectal and lung cancer. For prostate and breast cancer, life expectancy with cancer was longer at LTPA levels < median and ≥ median compared to no LTPA, although the confidence intervals for life expectancy with cancer at each level of LTPA overlapped.

6.3.3 TV viewing with colorectal, lung, prostate, and postmenopausal breast cancer life expectancy

Life expectancy cancer-free was longer for viewing TV sometimes and seldom/never compared to often/very often viewing TV for colorectal, lung, and breast cancer (Figure 10). Compared to often/very often viewing TV, viewing TV seldom/never was associated with a

greater cancer-free life expectancy of ~1 year for colorectal (men 1.2 years (95% CI 0.5, 1.9), women 1.2 years (95% CI 0.6, 1.9)), lung (men 1.4 years (95% CI 0.7, 2.0), women 1.4 years (95% CI 0.7, 2.1)), and breast cancer (women 1.4 years (95% CI 0.4, 2.4)) (Figure 10). However, for prostate cancer, seldom/never watching TV compared to often/very often was not associated with longer cancer-free life expectancy (0.5 years (95% CI -0.4, 1.3). Life expectancy with cancer was similar for each level of TV viewing for colorectal, lung, and breast cancer. For prostate cancer, life expectancy with cancer was longer for sometimes and seldom/never viewing TV compared to often/very often but the confidence intervals for life expectancy with cancer at each level of TV viewing overlapped.

6.3.4 Combined LTPA and TV viewing with colorectal, lung, prostate, and postmenopausal breast cancer life expectancy

For all types of cancer, participating in more LTPA and viewing less TV were associated in a dose-response fashion with life expectancy cancer-free (Figure 11). For colorectal, lung, and breast cancer, life expectancy cancer-free was greater by ~3 years for engaging in LTPA $\geq$ median and seldom/never viewing TV compared to the referent group of no LTPA and often/very often viewing TV (colorectal: men 3.2 years (95% CI 2.4, 4.0), women 3.3 years (95% CI 2.4, 4.1), lung: men 3.3 years (95% CI 2.5, 4.1), women 3.4 years (95% CI 2.5, 4.2), breast: 3.5 years (95% CI 2.2, 4.8)). This association was attenuated for prostate cancer with a life expectancy difference cancer-free of 2 years for LTPA $\geq$ median and seldom/never viewing TV compared to the referent group (1.9 years (95% CI 0.9, 3.0)).

6.4 Discussion

In this population-based cohort, engagement in any LTPA and viewing TV sometimes or seldom/never were associated with extended cancer-free life expectancy. Engagement in LTPA

showed a positive dose-response relationship with cancer-free life expectancy, such that at each level of LTPA participation life expectancy cancer-free was greater by approximately one year. Viewing TV sometimes or seldom/never was associated with a longer cancer-free life expectancy, but the magnitude of associations was more modest than those observed for LTPA. Cancer-free life expectancy findings were consistent for colorectal, lung, and breast cancer but weaker results were found with prostate cancer.

Engagement in more LTPA was associated with a lower incidence of colorectal, lung, and breast cancer but not prostate cancer. Our results on LTPA and cancer incidence are consistent with existing studies that have reported inverse associations with incident colorectal, lung, and breast cancer and mixed results for prostate cancer.[7, 74, 76, 78, 80] Our results also support the inverse association between greater LTPA and a reduced risk of all-cause mortality that has been reported by other cohort studies.[55, 115] Plausible biological mechanisms for how physical activity may reduce the risk of multiple cancers include reducing levels of adiposity, decreasing levels of sex and metabolic hormones, reducing systemic inflammation, improving immune function, and for colorectal cancer, improving colon motility.[91]

We observed a positive, graded relationship between LTPA and cancer-free life expectancy for all four types of cancer. For colorectal, lung, and breast cancer, at LTPA < median, life expectancy cancer-free was approximately 1 year greater, compared to no LTPA participation. At LTPA $\geq$ median, the life expectancy estimates were 2 years greater compared to no LTPA. For prostate cancer, the life expectancy cancer-free was weaker than the estimates observed with other types of cancers. This is most likely due to a null association of LTPA with cancer incidence but a strong inverse association with all-cause mortality. In contrast, for

colorectal, lung, and breast, LTPA had strong associations with both cancer incidence and all-cause mortality, and as a result the life expectancy cancer-free was greater for these cancers.

Our findings are consistent with those of other studies on physical activity and chronic disease-free life expectancy. Higher levels of physical activity compared to lower levels or none have been associated with a greater CVD-free life expectancy of 3 years,[10, 12] greater diabetes-free life expectancy of 4 years,[25] and greater chronic disease-free life expectancy of 3 years.[28] Our work complements these studies by examining four leading cancers types. Additionally, specifying LTPA as MET-h/week enhances the translation of our findings. One can reach 6.6 MET-h/week (midpoint of our lower LTPA category) and 13.7 MET-h/week by taking a brisk walk (at 3.3 METs) for 24 and 50 minutes/day for 5 days of the week.

In our analysis, TV viewing was not associated with any type of cancer. Current research suggests no association of TV viewing with breast cancer [8, 86] and prostate cancer [8, 85], mixed results for lung cancer,[83, 84] and an increased risk of colon cancer with more TV viewing.[8, 87, 121] Our null finding on TV viewing with colorectal cancer may be due to limited power to detect differences since we had 361 cases of colorectal cancer in our sample relative to more than 1,000 cases of colorectal cancer in previous studies on TV viewing.[87, 121] We observed that viewing TV sometimes or seldom/never was associated with a reduced risk of all-cause mortality, which is consistent with existing research.[61]

For most cancer states, viewing TV sometimes or seldom/never was associated with ~1 year gain in cancer-free life expectancy compared to often/very often watching TV. In our analysis, TV viewing was not associated with any incident cancers. However, viewing TV sometimes or seldom/never was protective against all-cause mortality; this association explains the gain in cancer-free life expectancy among those who watched less TV. Although

seldom/never viewing TV was associated with a lower risk of all-cause mortality in the prostate models, seldom/never viewing TV was associated with an increased risk of prostate cancer. The opposing direction for incidence and mortality likely explains why life expectancy prostate-free is similar by level of TV watching. We cannot exclude the possibility of residual confounding as a possible explanation for the observed increased risk of prostate cancer with less TV viewing.

Our study has a number of strengths, most importantly we used health expectancy metrics to examine how health behaviors influenced years lived cancer-free.[18] Additionally, our analyses included use of time-varying exposures and covariates to update behaviors as they changed throughout the observation period and well-measured and adjudicated outcomes. We addressed missing exposure and covariate data with multiple imputation techniques and conducted analysis with a prospective population-based cohort with 25 years of follow-up.

Despite the strengths of our study, limitations should be considered. We did not account for physical activity from travel, occupation, and housework and it is possible that the strength of observed associations would be greater if activity from multiple domains were included. LTPA may be overestimated by self-report, however, the Baecke questionnaire has good reliability and validity.[116, 117] Our measure of sedentary behavior, TV viewing, does not include time spent sitting for work or commuting. Additionally, the TV question assessed frequency of viewing but not the number of hours.

6.5 Conclusion

Engagement in any LTPA and sometimes or seldom/never viewing TV were associated with longer cancer-free life expectancy. Findings were similar for colorectal, lung, and breast cancer but weaker for prostate cancer. Our results suggest that engaging in more LTPA and less

TV viewing may contribute to living more years free of colorectal, lung, prostate, and breast cancer.

Table 12. Baseline characteristics of ARIC Study participants, n=14,508.

	Leisure-time physical activity			TV viewing			Overall
	None	< median	≥ median	Seldom/ never	Sometimes	Often/ very often	
	N=5615	N=4424	N=4446	N=2670	N=6779	N=5030	N=14,508
Age at V1, mean(SD)	54.4 (5.7)	54.4 (5.8)	54.7 (5.8)	54.0 (5.7)	54.4 (5.7)	54.9 (5.8)	54.3 (5.7)
Male, %	2312 (41.2)	1801 (40.7)	2454 (55.2)	1098 (41.1)	2905 (42.9)	2562 (50.9)	6582 (45.4)
ARIC center, n(%)							
Forsyth County	1175 (20.9)	1207 (27.3)	1297 (29.2)	705 (26.4)	1759 (26.0)	1213 (24.1)	3682 (25.4)
Jackson	2119 (37.7)	784 (17.7)	616 (13.9)	400 (15.0)	1634 (24.1)	1485 (29.5)	3536 (24.4)
Minneapolis	953 (17.0)	1269 (28.7)	1417 (31.9)	845 (31.7)	1644 (24.3)	1150 (22.9)	3640 (25.1)
Washington County	1368 (24.4)	1164 (26.3)	1116 (25.1)	720 (27.0)	1742 (25.7)	1182 (23.5)	3650 (25.2)
White, n(%)	3313 (59.0)	3465 (78.3)	3730 (83.9)	2224 (83.3)	4982 (73.5)	3296 (65.5)	10514 (72.5)
African American, n(%)	2302 (41.0)	959 (21.7)	716 (16.1)	446 (16.7)	1797 (26.5)	1734 (34.5)	3994 (27.5)
Education, n(%)							
high school or less	3771 (67.3)	2383 (53.9)	1984 (44.7)	1292 (48.5)	3747 (55.4)	3094 (61.6)	8155 (56.3)
vocational	414 (7.4)	405 (9.2)	385 (8.7)	215 (8.1)	566 (8.4)	422 (8.4)	1205 (8.3)
college	1019 (18.2)	1214 (27.5)	1443 (32.5)	818 (30.7)	1752 (25.9)	1106 (22.0)	3679 (25.4)
graduate/professional	399 (7.1)	418 (9.5)	627 (14.1)	341 (12.8)	705 (10.4)	398 (7.9)	1445 (10.0)
Missing	12	4	7	4	9	10	24
Leisure-time physical activity, n(%)							
no LTPA				849 (31.8)	2603 (38.4)	2161 (43.0)	5615 (38.8)
< median				805 (30.1)	2042 (30.1)	1575 (31.3)	4424 (30.5)
≥ median				1016 (38.1)	2134 (31.5)	1294 (25.7)	4446 (30.7)
Missing				0	0	0	23
TV viewing, n(%)							
seldom/never	849 (15.1)	805 (18.2)	1016 (22.9)				2670 (18.4)
sometimes	2603 (46.4)	2042 (46.2)	2134 (48.0)				6779 (46.8)
often/very often	2161 (38.5)	1575 (35.6)	1294 (29.1)				5030 (34.7)
Missing	2	2	2				29
Smoking, n(%)							
current smoker	1803 (32.1)	1058 (23.9)	890 (20.0)	543 (20.4)	1650 (24.4)	1557 (31.0)	3760 (25.9)
past smoker	1510 (26.9)	1409 (31.9)	1739 (39.2)	867 (32.5)	2153 (31.8)	1638 (32.6)	4665 (32.2)
never smoker	2298 (41.0)	1955 (44.2)	1812 (40.8)	1257 (47.1)	2974 (43.9)	1829 (36.4)	6071 (41.9)
Missing	4	2	5	3	2	6	12
Alcohol intake, n(%)							
not current drinker	3774 (67.7)	2707 (61.5)	2348 (53.1)	1621 (61.0)	4182 (62.0)	3020 (60.5)	8835 (61.3)
≤ 100 grams	1100 (19.7)	1124 (25.5)	1342 (30.4)	694 (26.1)	1672 (24.8)	1200 (24.0)	3566 (24.8)

	Leisure-time physical activity			TV viewing			Overall
	None	< median	≥ median	Seldom/ never	Sometimes	Often/ very often	
	N=5615	N=4424	N=4446	N=2670	N=6779	N=5030	N=14,508
> 100 grams	700 (12.6)	574 (13.0)	731 (16.5)	344 (12.9)	887 (13.2)	774 (15.5)	2007 (13.9)
Missing	41	19	25	11	38	36	100
BMI, mean (SD)	28.7 (6.0)	27.4 (5.2)	26.9 (4.6)	26.9 (5.0)	27.7 (5.4)	28.3 (5.6)	27.8 (5.4)
Missing	6	3	2	2	2	7	23
Menopausal Hormone Therapy, n(%)							
current user of unopposed estrogen	409 (13.1)	335 (13.3)	276 (14.4)	194 (12.8)	512 (13.9)	314 (13.3)	1020 (13.5)
current user of estrogen + progestin	103 (3.3)	154 (6.1)	165 (8.6)	114 (7.5)	220 (6.0)	88 (3.7)	422 (5.6)
never used	2194 (70.2)	1650 (65.5)	1175 (61.5)	983 (65.0)	2440 (66.3)	1592 (67.5)	5019 (66.4)
former user of any type	421 (13.5)	380 (15.1)	296 (15.5)	222 (14.7)	511 (13.9)	364 (15.4)	1097 (14.5)
Missing	147	80	56	42	158	83	291
Postmenopausal, n(%)	2948 (90.0)	2303 (88.6)	1730 (87.9)	1322 (85.0)	3427 (89.2)	2228 (91.3)	6988 (89.0)
Missing	0	0	0	0	0	0	0
Daily serve red meat intake, mean (SD)	1.2 (1.0)	1.1 (0.8)	1.0 (0.8)	1.0 (0.8)	1.1 (0.8)	1.2 (1.0)	1.1 (0.9)
Missing	12	4	11	1	16	10	42

Abbreviations: BMI= body mass index, LTPA= leisure-time moderate-to-vigorous physical activity, MET= metabolic equivalent of task
LTPA categories: < median (0.1 - < 13.2 MET-h/week), ≥ median (13.2+ MET-h/week)

Table 13. Associations (hazard ratio, 95% CI) of leisure-time physical activity with colorectal, lung, prostate, and breast cancer (disease) and all-cause mortality (death) among ARIC Study participants (1987 - 2012).

	health to disease	health to death HR (95% CI)	disease to death
Colorectal			
Number of events	361	4,870	184
Total person-years	304,961	304,961	2,618
LTPA			
None	ref	ref	ref
< median	0.98(0.75,1.29)	0.86(0.80,0.93)	0.85(0.56,1.28)
≥ median	0.81(0.62,1.06)	0.75(0.69,0.80)	1.19(0.82,1.73)
Lung			
Number of events	560	4,572	482
Total person-years	306,286	306,286	1,292.21
LTPA			
None	ref	ref	ref
< median	0.88(0.70,1.09)	0.87(0.81,0.94)	0.80(0.58,1.10)
≥ median	0.84(0.68,1.04)	0.75(0.70,0.81)	0.93(0.71,1.22)
Prostate			
Number of events	813	2,475	300
Total person-years	127,060	127,060	7,462
LTPA			
None	ref	ref	ref
< median	1.12(0.92,1.37)	0.90(0.81,1.00)	1.00(0.74,1.37)
≥ median	1.00(0.84,1.19)	0.78(0.70,0.86)	0.86(0.64,1.15)
Breast			
Number of events	564	2,041	215
Total person-years	163,389	163,389	5,401
LTPA			
None	ref	ref	ref
< median	0.97(0.78,1.19)	0.83(0.74,0.93)	0.65(0.47,0.91)
≥ median	0.84(0.67,1.05)	0.73(0.64,0.83)	0.54(0.37,0.79)

LTPA categories: < median (0.1 - < 13.2 MET-h/week), ≥ median (13.2+ MET-h/week)
Colorectal cancer and lung cancer models N=14,508, prostate cancer models N=6582, and breast cancer models N=7849
Models specified separately for each type of cancer.
Models adjusted for age, gender, race by ARIC center, education, smoking status, and alcohol intake. Prostate and breast models do not include gender.
Abbreviations: HR= hazard ratio, CI = confidence interval, LTPA= leisure-time moderate-to-vigorous physical activity, MET= metabolic equivalent of task

Table 14. Associations (hazard ratio, 95% CI) of TV viewing with colorectal, lung, prostate, and breast cancer (disease) and all-cause mortality (death) among ARIC Study participants (1987 - 2012).

	health to disease	health to death HR (95% CI)	disease to death
Colorectal			
Number of events	361	4,870	184
Total person-years	304,961	304,961	2,618
TV viewing			
Often/very often	ref	ref	ref
Sometimes	1.05(0.83,1.32)	0.89(0.84,0.95)	0.79(0.57,1.11)
Seldom/never	0.96(0.70,1.31)	0.85(0.78,0.93)	0.93(0.59,1.46)
Lung			
Number of events	560	4,572	482
Total person-years	306,286	306,286	1,292.21
TV viewing			
Often/very often	ref	ref	ref
Sometimes	1.07(0.89,1.29)	0.87(0.82,0.93)	1.09(0.87,1.35)
Seldom/never	1.09(0.85,1.40)	0.82(0.75,0.90)	1.32(0.99,1.75)
Prostate			
Number of events	813	2,475	300
Total person-years	127,060	127,060	7,462
TV viewing			
Often/very often	ref	ref	ref
Sometimes	1.07(0.92,1.25)	0.92(0.85,1.01)	0.85(0.66,1.09)
Seldom/never	1.20(0.99,1.47)	0.86(0.76,0.97)	0.96(0.69,1.33)
Breast			
Number of events	564	2,041	215
Total person-years	163,389	163,389	5,401
TV viewing			
Often/very often	ref	ref	ref
Sometimes	0.95(0.78,1.15)	0.86(0.78,0.94)	0.94(0.69,1.28)
Seldom/never	1.03(0.81,1.30)	0.80(0.70,0.92)	1.05(0.71,1.54)

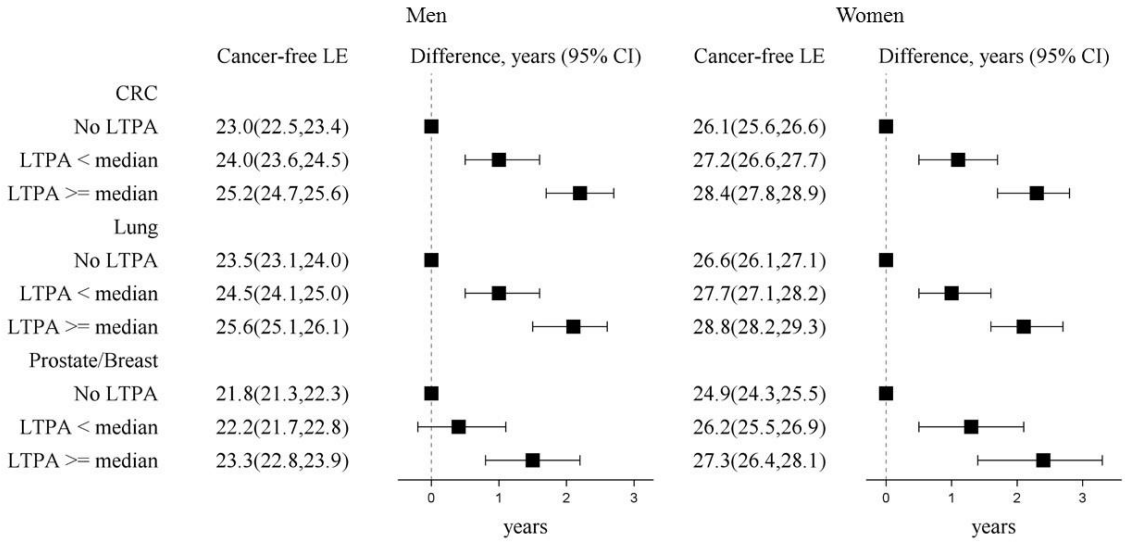
Colorectal cancer and lung cancer models N=14,508, prostate cancer models N=6582, and breast cancer models N=7849

Models specified separately for each type of cancer.

Models adjusted for age, gender, race by ARIC center, education, smoking status, and alcohol intake. Prostate and breast models do not include gender.

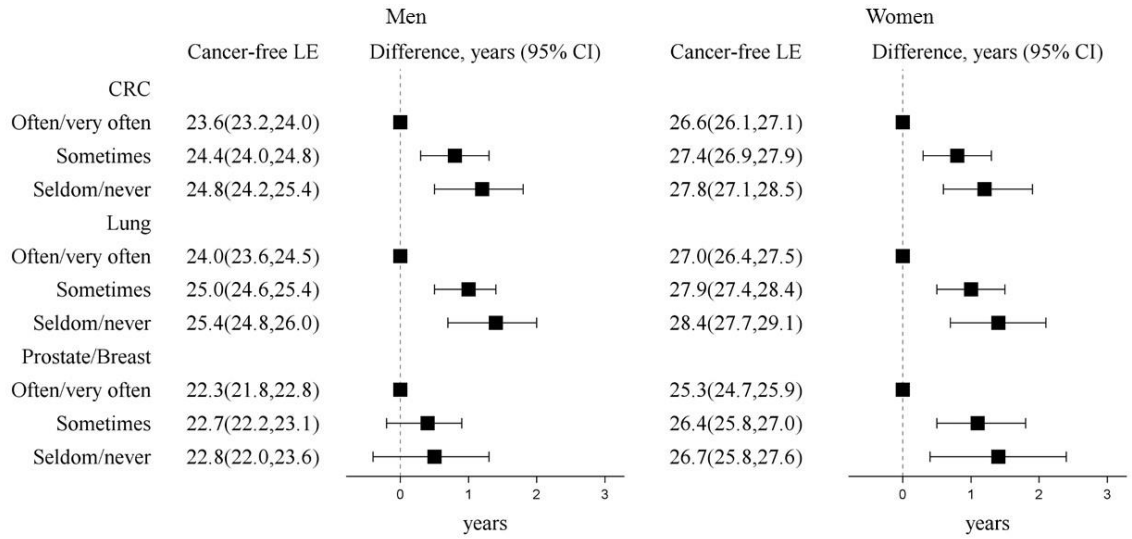
Abbreviations: HR= hazard ratio, CI = confidence interval

Figure 9. Life expectancy (years, 95% CI) free of cancer and life expectancy differences at age 50 by LTPA among ARIC Study participants (1987 - 2012).



LTPA categories: < median (0.1 - < 13.2 MET-h/week), ≥ median (13.2+ MET-h/week)
Colorectal cancer and lung cancer models N=14,508, prostate cancer models N=6582, and breast cancer models N=7849
Models specified separately for each type of cancer.
Models adjusted for age, gender, race by ARIC center, education, smoking status, and alcohol intake. Prostate and breast models do not include gender.
Abbreviations: CI = confidence interval, CRC= colorectal cancer, LE= life expectancy, LTPA=leisure-time moderate-to-vigorous physical activity, MET= metabolic equivalent of task

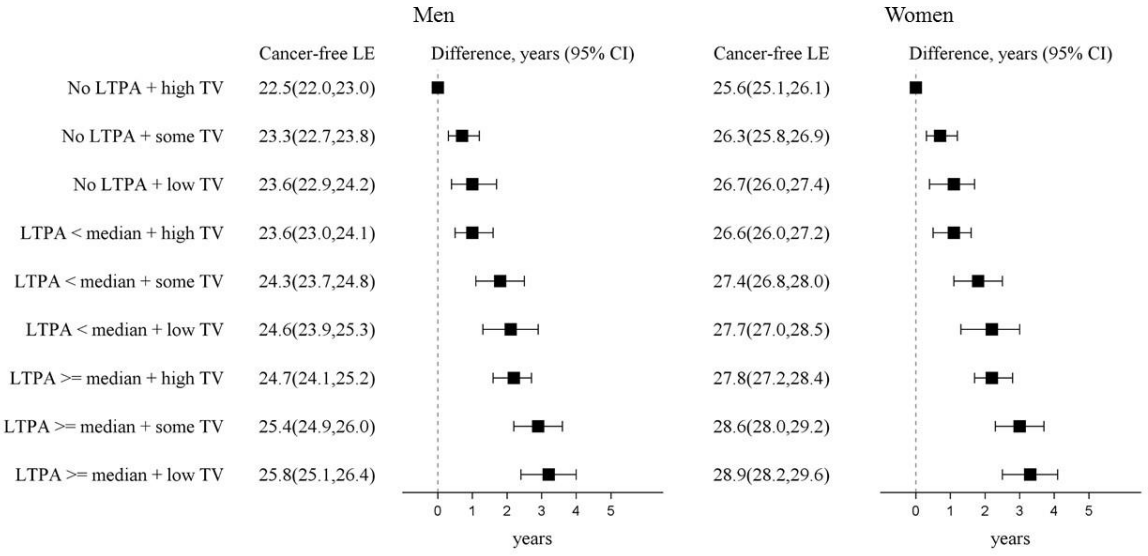
Figure 10. Life expectancy (years, 95% CI) free of cancer and life expectancy differences at age 50 by TV among ARIC Study participants (1987 - 2012).



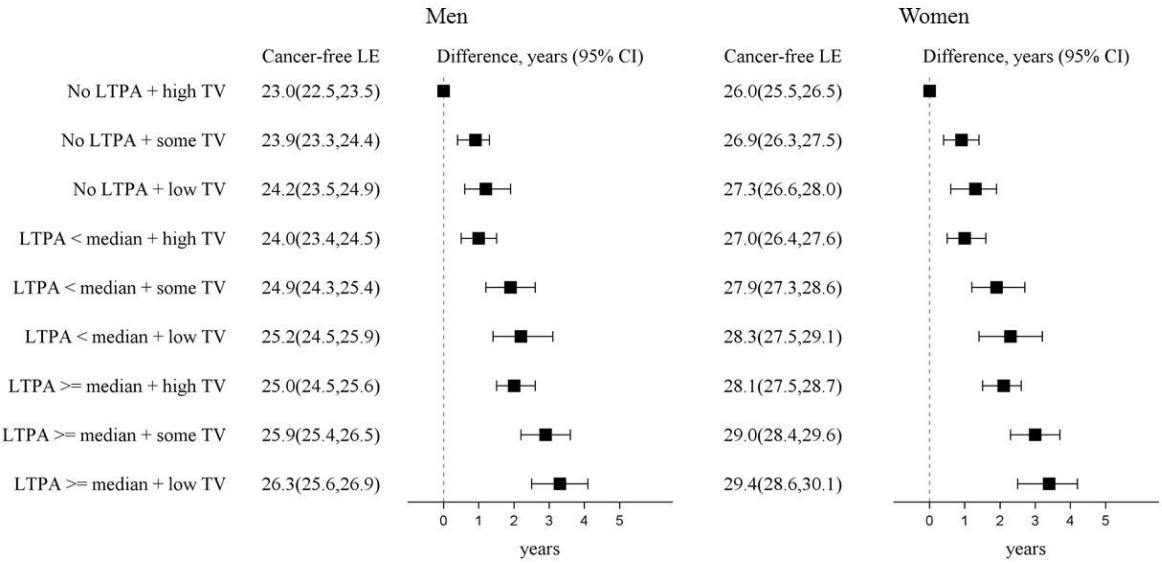
Colorectal cancer and lung cancer models N=14,508, prostate cancer models N=6582, and breast cancer models N=7849
Models specified separately for each type of cancer.
Models adjusted for age, gender, race by ARIC center, education, smoking status, and alcohol intake. Prostate and breast models do not include gender.
Abbreviations: CI = confidence interval, CRC= colorectal cancer, LE= life expectancy

Figure 11. Life expectancy (years, 95% CI) free of cancer and life expectancy differences at age 50 by LTPA and TV viewing among ARIC Study participants (1987 - 2012).

3a) Colorectal cancer

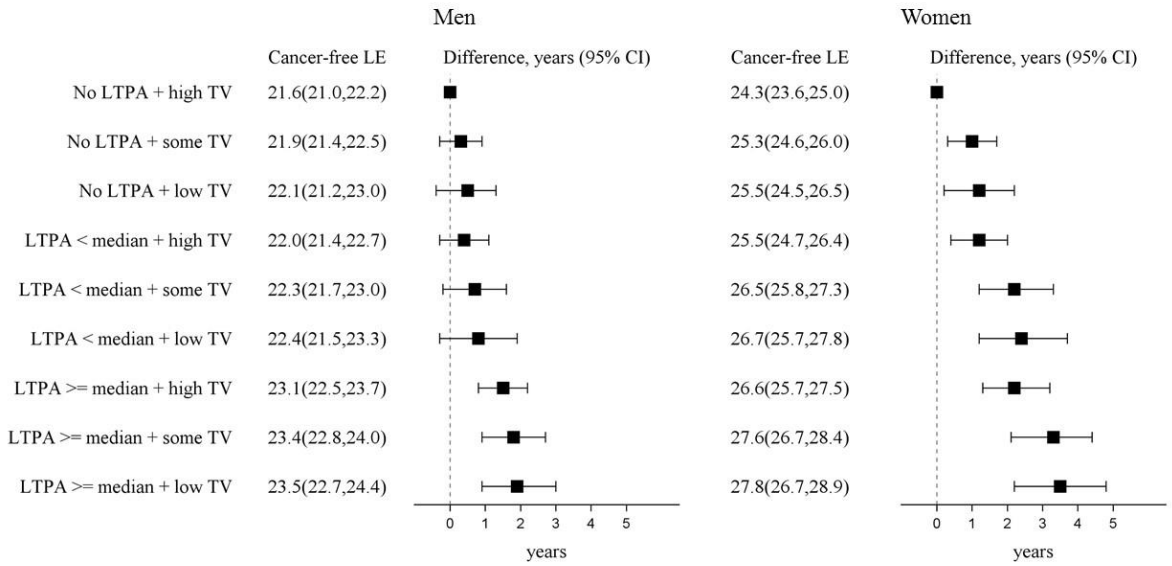


3b) Lung cancer



3c) Prostate cancer

3d) Breast cancer



Colorectal cancer and lung cancer models N=14,508, prostate cancer models N=6582, and breast cancer models N=7849
LTPA categories: < median (0.1 - < 13.2 MET-h/week), ≥ median (13.2+ MET-h/week)
TV categories: high TV is viewing often/very often, some TV is sometimes viewing, and low TV is seldom/never viewing TV.
Models specified separately for each type of cancer.
Models adjusted for age, gender, race by ARIC center, education, smoking status, and alcohol intake. Prostate and breast models do not include gender
Abbreviations: CI = confidence interval, CRC= colorectal cancer, LE= life expectancy, LTPA=leisure-time moderate-to-vigorous physical activity, MET= metabolic equivalent of task.

CHAPTER 7: CONCLUSIONS AND PUBLIC HEALTH IMPLICATIONS

7.1 Summary of findings

This doctoral research investigated how physical activity and sedentary behavior are associated with life expectancy free of seven leading chronic diseases. The findings suggest that engaging in physical activity and sedentary behavior can influence the number of years lived in health.

The association of physical activity with nonfatal CVD and cancer

Participation in LTPA $\geq$ median in the past year compared to none was associated with a reduced risk of three nonfatal CVDs - CHD, stroke, and HF - and three types of cancer - colorectal, lung, and breast. LTPA was not associated with prostate cancer. We observed an inverse dose-response relationship between LTPA and all-cause mortality in the absence of having each of these diseases in both the CVD and cancer analyses. The association between LTPA and all-cause mortality after developing these diseases was less clear. For example, engaging in LTPA $\geq$ median compared to none was associated with a lower risk of all-cause mortality after developing nonfatal CHD and HF and postmenopausal breast cancer, but no clear pattern was observed for the other diseases. Our results on the association of physical activity with incident CVD and cancer, and with all-cause mortality, are consistent with prior research in these areas. These results suggest that engagement in more LTPA is associated with a lower risk of developing various types of CVD and cancer, and a lower risk of all-cause mortality in the absence of having these diseases.

The association of physical activity with nonfatal CVD- and cancer-free life expectancy

LTPA was associated in a positive dose-response fashion with extending life expectancy free of nonfatal CVD and three forms of cancer. Compared to no LTPA, participating in LTPA < median and ≥ median was associated with a longer nonfatal life expectancy CVD-free by ~1 and ~2 years, respectively. This was similar for nonfatal CHD, stroke, and HF. The cancer-free life expectancies by level of LTPA also showed a very similar dose-response relationship. Compared to no LTPA, life expectancy free of colorectal-, lung-, and breast cancer were longer by 1 year and more than 2 years for engaging in LTPA < median and ≥ median. The results were weaker for prostate cancer, such that at LTPA levels < median the life expectancy gain was 0.1 years and at LTPA levels ≥ median the gain was 1.1 years longer compared to no LTPA. The weaker results for prostate cancer are most likely due to a null association of LTPA with prostate cancer incidence but an inverse association with all-cause mortality. In contrast, for all other disease states, LTPA had a strong inverse association with both disease incidence and all-cause mortality. These results suggest that engaging in more LTPA may contribute to more years spent free of some of the leading chronic diseases.

The association of sedentary behavior with nonfatal CVD and cancer

Viewing TV seldom/never compared to often/very often was associated with a reduced risk of nonfatal CHD and HF; TV viewing was not associated with any of the other diseases. In both the CVD and cancer analyses, watching TV sometimes or seldom/never compared to often/very often was associated with a lower risk of all-cause mortality in the absence of these diseases. Also consistent with each analysis was a null association of TV viewing with all-cause mortality after developing each type of CVD and cancer.

The association of sedentary behavior with nonfatal CVD- and cancer-free life expectancy

Viewing TV sometimes or seldom/never was associated with a longer nonfatal CVD- and cancer-free life expectancy. For all types of CVD, the nonfatal life expectancy CVD-free was greater by ~0.8 years for viewing TV sometimes and seldom/never compared to often/very often viewing TV. For the different types of cancer, a similar relationship was observed for colorectal, lung, and breast cancer with a longer cancer-free life expectancy ~1 year and ~1.4 years for sometimes and seldom/never viewing TV compared to often/very often viewing, respectively. These findings suggest viewing less TV may be associated with longer life expectancy free of many types of CVD and cancer.

The one exception was prostate cancer for which the life expectancy prostate cancer-free was similar for each level of TV. Although seldom/never viewing TV was associated with a lower risk of all-cause mortality in the prostate models, seldom/never viewing TV was also associated with an increased risk of prostate cancer. The opposing direction for incidence and mortality likely explains why life expectancy prostate-free is similar by level of TV watching. We cannot exclude the possibility of residual confounding as a possible explanation for the observed increased risk of prostate cancer with less TV viewing.

7.2 Strengths

This dissertation has as number of strengths, which include the examination of seven chronic diseases, the inclusion of sedentary behavior, specifying physical activity as MET-h/week, use of time varying exposures and covariates, and multiple imputation of missing data.

To our knowledge, this is the only study to separately examine how physical activity is associated with cancer life expectancy outcomes. To date, research in area of physical activity with health expectancy outcomes has primarily addressed CVD and composite chronic disease

outcomes. The inclusion of cancer is an important innovation as it is one of the leading causes of death, premature mortality, and years lived with disability.[118] This research highlights how engaging in more physical activity and viewing less TV are associated with living more years free of four types of cancer.

We also examined whether sedentary behavior is associated with nonfatal CVD and cancer life expectancy outcomes. Many health behaviors and conditions (obesity, smoking, alcohol) have been examined with CVD life expectancy outcomes but none have investigated sedentary behavior.[10, 11] In this analysis we observed that viewing TV sometimes or seldom/never was associated with greater life expectancy CVD and cancer-free compared to often/very often viewing TV. This is important as sedentary behavior is highly prevalent and Americans are sedentary on average 8 hours per day.[50] Our results suggest less frequent TV watching may extend disease-free life expectancy but future research should use a different measure of sedentary behavior if possible, such as hours spent sitting.

In both the CVD and cancer analysis, we measured physical activity expenditure in MET-h/week, which enhances the translation of our findings. By using a standardized metric, our results can be replicated and compared with other cohorts that use MET-h/week of physical activity.

As a further strength, in both the CVD and cancer analyses we had extensive follow-up time of close to 30 and 25 years, respectively. We accounted for changes in behavior that occurred over follow-up by using time-varying exposures and covariates. To address missing exposure and covariate data we used multiple imputation techniques, which limited loss to sample size and potentially reduced bias that may have occurred with a complete case analysis.

7.3 Limitations

This research is subject to several limitations, one of which is the use of one domain of physical activity and sedentary behavior. We included physical activity that occurred during leisure-time and did not include physical activity that occurred during work, from doing household activities, or while commuting. The addition of physical activity from these other domains may have strengthened the observed associations.

Our measure of sedentary behavior was based on a question about TV viewing, which omits sedentary behavior that occurs while at work or during travel. Furthermore, this question did not able to capture the number of hours spent watching TV, but only the frequency.

Both physical activity and TV viewing were self-reported. Physical activity tends to be overestimated when self-reported, but the reliability and validity of the Baecke questionnaire is similar in reliability and validity as other physical activity questionnaires.[116, 117] The questions used to ascertain TV viewing from the Baecke questionnaire have not been compared specifically against other TV watching measures; however, other validation and reliability studies of sedentary questions suggest reliability is high but validity varies for domain-specific sedentary behavior (TV viewing, sitting at work).[122, 123] For example, in one study both reliability and validity (measured as intra-class correlations (ICC)) were moderate to high (reliability ICC ranged from 0.65 to 0.86 and validity ICC ranged from 0.53 to 0.77) for both sitting at work and watching TV.[122]

7.4 Public health significance

CVD and cancer are leading chronic diseases; over 92.1 million of living Americans have been diagnosed with CVD[30] and 15.5 million have a cancer history.[32] The results from this dissertation suggest that increasing LTPA levels and limiting TV viewing will likely reduce the

incidence of some types of CVD and cancer, lower the risk of all-cause mortality, and extend the number of years lived free of CVD and cancer. Based on this observational prospective study, it is likely that if population physical activity levels increased and sedentary behavior levels decreased, fewer people would develop certain types of CVD and cancer and more years of life would be spent in health rather than managing morbidity related to these types of conditions. Although we lack experimental confirmation of our results, it can be posited that promoting physical activity and reducing sedentary behavior have the potential to help millions of Americans maintain and improve their health.

Life expectancy disease-free, the metric used in this dissertation, is easily understood and may be an effective motivational tool for behavior change. Presenting information on the number of years one can expect to live healthy, or free of certain chronic diseases, is likely to be of interest to many people. In support of this, from interviews with older adults from two US aging cohorts, one of the most important priorities mentioned by participants regarding aging was to remain in good health until close to death. [124]

This metric targets individual level behavior change. Although individual level behavior change is important for increasing physical activity, factors at multiple levels of the environment also need to be addressed to have a substantial public health impact on increasing population levels of physical activity and decreasing sedentary behavior levels. Several physical activity interventions that target community settings, school settings, workplaces, families and the home environment, and coordinated environmental interventions have been effective at increasing physical activity levels among many population groups.[125-129] Conveying the message of how physical activity and TV viewing impact the number of years one can expect to live healthy, or

free of certain chronic diseases, can be part of a holistic multi-pronged approach to optimize the population levels of these behaviors.

7.5 Future Directions

The findings from this dissertation point to several future directions of research. First, this type of research should be replicated in other cohorts, especially ones that have a range of participants that are diverse in race/ethnicity and socio-economic status. Many demographic and social factors influence disease incidence and mortality risk and it is likely that the magnitude of life expectancy estimates will vary between cohorts due to differences in demographic, social factors, and risk factor burden. To further the work on cancer, conducting analysis with consortiums would increase the types and number of cancer cases to be investigated.

Second, additional analyses on physical activity and life expectancy outcomes could include activity that occurs in various domains (household, work, leisure-time, commuting). It would also be advantageous for future research to include regular assessments of physical activity to update changes in physical activity participation throughout the observation period. Additionally, accelerometers could be used to examine how objective measures of physical activity are associated with disease-free life expectancy. This type of analysis could, in addition to examining moderate-to-vigorous intensity physical activity, also investigate how light intensity and number of steps are associated with disease-free life expectancy outcomes. Limited research suggests that number of steps may be inversely associated with incident CVD.[130] Additionally, greater amounts of light intensity activity may be associated with lower CVD risk.[131] Similar to physical activity, other measures of sedentary behavior should be used in future research on disease-free life expectancy outcomes. Self-reported measures of total sitting

time or accelerometer measured sedentary time could be further informative in addition to our single measure of TV viewing frequency.

Third, in this dissertation we focused on two modifiable behaviors, but research suggests that engaging in multiple health behaviors has been associated with longer life expectancy,[132] a lower risk of CVD,[133] a reduced risk of cancer,[134, 135] and longer CVD-free life expectancy.[10, 11] For example, in one study on CVD-free life expectancy, participants with a favorable risk profile based on smoking, physical activity, BMI, and alcohol intake had a longer CVD-free life expectancy of 8 to 13 years compared to participants with an unfavorable risk profile.[10] This dissertation research thus could be extended to include multiple health behaviors or use the American Heart Association's Life Simple 7 metric (smoking, body mass index, physical activity, diet, total cholesterol, blood glucose, blood pressure) to examine how each individual behavior and a combined number of health behaviors influence life expectancy free of CVD and cancer.

Fourth, health expectancy outcomes can be used to monitor trends in life expectancy in good and poor health over time. The European Union (EU) has used three types of life expectancy measures based on questions about activity limitations, chronic morbidity, and perceived health to monitor trends since 2004 in 28 EU member states.[136] In the US, the Centers for Disease Control and Prevention (CDC) published life expectancy at age 65 in good and poor self-rated health.[137] The CDC used data from the National Vital Statistics System, the Census Bureau, and the Behavioral Risk Factor Surveillance Study. These data inputs were used with modified life tables to partition life expectancy into good and poor self-rated health.[137] It may be possible to extend these types of analyses into life expectancy with and without disease based on current mortality data and self-reported diseases (such as CVD and cancer) with the use of

nationally representative studies, such as NHANES or the National Health Interview Survey. In these types of analyses, life expectancy with and without disease could be examined over time and by demographic factors to monitor population health.[138]

7.6 Conclusions

Engagement in any LTPA compared to none was associated with a longer disease-free life expectancy for all CVDs and cancer types. For example, engaging in LTPA greater than or equal to the median compared to no LTPA was associated with a longer disease-free life expectancy of ~1.5 years for CHD, ~1.8 years for stroke, ~1.6 years for HF, ~2.2 years for colorectal, ~2.1 years for lung, ~1.5 years for prostate, and ~2.4 years for postmenopausal breast cancer. Viewing TV sometimes or seldom/never compared to often/very often viewing was associated with longer CVD and cancer-free life expectancy of ~1 year for all diseases except for prostate cancer. In comparison to LTPA, the life expectancy differences by level of TV were more modest than the differences by level of LTPA. Our results suggest that engaging in more LTPA and viewing less TV may contribute to living longer free of many of the leading chronic diseases.

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