PHYSICAL ACTIVITY AND SEDENTARY BEHAVIOR IN THE CANCER PREVENTION STUDIES

by

ERIKA REES

(Under the Direction of Ellen M. Evans)

ABSTRACT

Substantial evidence suggests that physical inactivity is associated with cardiovascular disease, certain types of cancer, and premature death. Distinct from physical inactivity, sedentary time (characterized by very low energy expenditure while sitting/lying) is independently associated with these adverse outcomes. Measuring physical activity (PA) and sedentary behavior (SED) remains a challenge, particularly in large epidemiologic cohorts where surveys are the most common measurement method. This study aimed to: 1) evaluate the test-retest reliability and criterion validity of the Cancer Prevention Study-3 (CPS-3) PA and SED surveys and 2) estimate the mortality risk reductions associated with replacing 30 $\text{min}\cdot\text{day}^{-1}$ SED with an equivalent amount of light intensity PA (LPA) or moderate-to-vigorous intensity PA (MVPA) in the Cancer Prevention Study-II Nutritional Cohort (CPS-II). The validation studies included 713 participants aged 31-72 years. Reliability was assessed by computing Spearman correlation coefficients between pre- and post-study survey responses. Validity was assessed by comparing PA and SED estimated from the CPS-3 survey with accelerometry and seven-day diaries. Reliability was acceptable or strong for all CPS-3 items and validity estimates were comparable to studies of PA/SED questionnaires with similar survey characteristics. Together, these findings suggest that the CPS-3 survey is suitable for ranking or categorizing participants according to PA or SED time. The mortality study included 101,757 participants aged 69.0±6.2 years. An isotemporal substitution approach to Cox proportional hazards regression was used to estimate adjusted hazard ratios and 95% confidence intervals (HR, 95% CI) for mortality associated with the substitution of 30 min·day^{-1} SED for LPA or MVPA. Overall, 31,801 participants died during 13 years of follow-up. Among the least active participants, the replacement of 30 min·day^{-1} SED with LPA was associated with a 14% mortality risk reduction (HR=0.86, 0.83-0.89) and replacement with MVPA was associated with a 50% mortality risk reduction (HR=0.50, 0.44-0.58). Similar associations were seen among moderately active participants (HR=0.91, 0.89-0.96 LPA replacement, HR=0.65, 0.56-0.79 MVPA replacement), but were not significant for the most active participants (HR=1.00, 0.97-1.02 LPA, HR=0.97, 0.95-1.01 MVPA). These findings suggest that replacing modest amounts of SED with even light intensity PA may improve health among less active people.

INDEX WORDS: Light intensity physical activity, Sitting time, Mortality, Validity, Reliability, CPS-II, CPS-3

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DEDICATION

To my parents, Denny and Wendy Rees, for imparting a suitable balance of ‘Midwest nice’ and ‘Midwestern grit’.

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CHAPTER 1

INTRODUCTION

1.1. Brief Overview

Decades of compelling research suggests that a lack of physical activity (PA) increases the risk of cardiovascular disease, type II diabetes, certain cancers, weight gain, and premature mortality.(1-3) Sedentary behavior (SED), characterized by an energy expenditure ≤1.5 metabolic equivalents while in a sitting, reclining, or lying position,(4) has more recently emerged as a risk factor for chronic disease independent of moderate-to-vigorous physical activity (MVPA).(5-12) It has become increasingly clear that replacing excess SED with more physically active behaviors may maximize health benefits. As evidence of the adverse effects of inactive and sedentary lifestyles accumulates, it is of upmost importance to assure that these exposures are accurately measured.

This dissertation includes three studies: 1) a validation study of the Cancer Prevention Study-3 (CPS-3) sitting time survey items, 2) a validation study of the CPS-3 PA items, and 3) an isotemporal substitution model of the mortality benefits for replacing sedentary time with physical activity. As the two validation studies share similar methods and utilize the same dataset, while the isotemporal substitution analysis study is distinct both in methodology and data source, chapters one and two will include two sub-sections: one section for the two validation studies and another for the study of mortality risk reductions for replacing SED.

1.2. Significance, Validation Studies

Much of the evidence for the health benefits of PA and limited SED comes from large prospective epidemiological studies. Historically, many epidemiological studies have relied on self-reported measures of activity exposures as they are lower in cost and typically less burdensome for both participants and researchers. While subjective measures remain the most feasible option for large-scale studies, their use may be limited by participant comprehension, difficulty recalling events, or other sources of measurement error.(13) To assess and limit the influence of such issues, studies must be conducted to evaluate the validity (the extent to which a measure represents true events; free from error or bias) and reliability (the extent to which a tool results in measures that are consistent and stable) of a measure.(14) Valid and reliable measures are necessary for accurately and consistently describing an exposure and understanding the presence and strength of associations observed in epidemiologic studies.

The CPS-3 activity validation studies will assess the potential impact of measurement error associated with the SED and PA questionnaire items. Results from these studies will not only allow for a better understanding of study estimates within CPS-3 and ease comparability of findings from other cohorts, but will also inform survey design and selection decisions for future epidemiologic studies of PA and SED. Results will assure that the CPS-3 SED and PA items are appropriate not only for the general U.S. population, but also for various demographic sub-groups.

1.3. Specific Aims, Validation Studies

Primary aims for the two validation studies are to evaluate a) the criterion validity of the CPS-3 sitting time survey items, b) the one-year test-retest reliability of the specific sitting time survey items, and c) the validity and reliability estimates of the sedentary behavior survey items by sex and race/ethnicity, and similarly, evaluate a) the criterion validity of the CPS-3 light, moderate, vigorous, and moderate-to-vigorous intensity physical activity survey items, b) the one-year test-retest reliability of the specific physical activity survey items, and c) the validity and reliability estimates of the physical activity survey items by sex and race/ethnicity.

Secondary aims include a) stratifying validity and reliability estimates by age, BMI, educational attainment, occupational status, and adherence to the 2008 physical activity guidelines for Americans (based on accelerometer data).

1.4. Significance, Study of Mortality Risk Reductions for Replacing Sedentary Time

Regular PA is associated with a lower risk of cardiovascular disease, type II diabetes, certain types of cancer, and premature death.(1-3) Further, it is estimated that an insufficient PA level, referred to as physical inactivity, is responsible for between 6-10% of the world’s burden of chronic diseases.(15) Distinct from physical inactivity, the amount of time spent engaging in SED, characterized by very low energy expenditure ($\leq$1.5 METs) while in a sitting, reclining, or lying position, is also associated with a higher risk of premature death and chronic disease, independent of physical inactivity.(5, 6, 8, 9, 12, 16) Largely due to technologic advancements in leisure and occupational time, Americans have become less active and more sedentary over recent decades. Americans currently spend at least 7.7 wakeful hours/day sedentary.(17)

While awake, a person is either sedentary or physically active at a light, moderate, or vigorous intensity. Because there is a finite amount of wakeful time in a day, additional time spent on one active or sedentary behavior displaces time spent on another.(18) Up until more recently, most studies explored the associations of SED and various health outcomes without considering the physical activities being displaced. This has left a gap in our understanding of healthful proportions of activity time, as it is not yet entirely clear if sedentary time must be replaced with MVPA to be beneficial, or if replacement with light intensity physical activities may be similarly beneficial. The application of an isotemporal substitution model (ISM) allows for the estimation of the effect of replacing SED time with time-matched physical activities.(19, 20)

This study will extend the work previously done in the Cancer Prevention Studies-II Nutrition Cohort showing that sitting time is positively associated and PA is inversely associated with premature mortality, and will contribute to the understanding of the associations between the proportion of time spent physically active or sedentary and the risk of premature mortality through the application of an ISM.

1.5. Specific Aims, Study of Mortality Risk Reductions for Replacing Sedentary Time

The primary aim of this study is to estimate the all-cause mortality risk reductions associated with replacing thirty minutes of total SED time with thirty minutes of either LPA or MVPA. Secondary aims include: 1) estimate the mortality risk reductions associated with replacing thirty minutes of daily sedentary time with time-matched LPA or MVPA among low, moderate, and high active participants separately, 2) estimate associations for all-cause, cardiovascular disease, cancer, and other causes of mortality, and 3) examine mortality risk reduction stratified by sex, body mass index (BMI) and age group.

CHAPTER 2

LITERATURE REVIEW

2.1. Importance of Validity and Reliability in Physical Activity and Sedentary Time Surveys

Exposure measures must be reliable and valid to consistently and accurately describe an exposure and to best understand the presence and strength of associations with health outcomes observed in epidemiologic studies. For a measure to be valid, or represent the ‘true’ scientific value, it must also be reliable, resulting in consistent and stable scores.(14) As physical and sedentary activities are complex, multi-dimensional behaviors, estimating measure validity and reliability remains a challenge.

Device-based measures of PA and SED, such as accelerometers and inclinometers, can provide valid estimates of ambulatory physical activity through the measurement of body acceleration.(21, 22) However, due to the ease of administration, relatively low cost, and low participant burden, many epidemiologic studies use self-reported measures of PA and SED time. Very few large cohorts can feasibly incorporate objective measures of PA and SED time, highlighting the need for valid self-reported instruments.

A variety of recall PA questionnaires have been developed over recent years. These questionnaires vary in the time frame queried, domains assessed, intensities assessed, and metric evaluated (for example, minutes of MVPA, rank-order of behavioral activity level, or mode of activity participation). Questionnaires are prone to social desirability (desire to intentionally misreport) and recall biases, and often overestimate PA level while underestimating sitting time.(23) Using accelerometers as the criterion, median validity coefficients of the most common physical activity questionnaires range from 0.25-0.41. However, questionnaires that appear to be valid in one population are not necessarily valid in others. As a result, validity estimates can vary significantly across race/ethnicity, country of origin, sex, age, BMI, and PA intensity assessed.(23, 24)

The PA and SED time items from the Cancer Prevention Study-3 (CPS-3) questionnaire were adopted from the California Teacher's Study (CTS) and the National Institutes of Health-AARP Diet and Health Study (NIH-AARP) Nutrition Cohort surveys. While the CTS and NIH-AARP are both well-established, large prospective studies of cancer incidence and mortality, neither of the study's PA or SED time surveys have been formally validated, further demonstrating the importance of validating the CPS-3 survey.

The lack of any simple gold standard for measuring PA and SED is a limitation of most validation studies. While accelerometers are appropriate for measuring the velocity of ambulatory bodily movements, they do not aptly measure non-ambulatory activities and often produce results which are highly influenced by data processing and proper wear. Perhaps more importantly, the measurement error associated with accelerometry and recall surveys may be correlated. This can be problematic as traditional validation approaches (for example, correlations between two measures) require independent measurement error between the two measures. The addition of a third measure can reduce this limitation when linear relationships between a latent 'true' PA measure and the amount measured by three independent instruments are assumed; this methodology is referred to as the method of triads.(25-28)

The method of triads has been used extensively in psychological and nutritional epidemiologic validation studies.(29-34) Although the method of triads is not as common in PA survey validation studies, it can realistically be applied in the validation of any continuous exposure measure. This methodology was used to estimate the one-year test-retest reliability and the criterion validity for minutes of weekly activity by intensity for the PA and SED time items in the CPS-3 survey.(13, 14)

2.2. Cancer Prevention Study-3 Activity Validation Sub-Study

The CPS-3 is a prospective study of cancer incidence and mortality initiated by the American Cancer Society (ACS). Participants were recruited at ACS fundraising events (e.g. Relay for Life, Making Strides Against Breast Cancer, etc.) or community enrollment drives between 2006 and 2013. Participants were considered for inclusion if they were between the ages of 30 and 65 with no history of cancer (except for basal or squamous cell skin cancer). Participants completed a baseline survey at enrollment and continue to receive follow-up surveys every three years. CPS-3 has over 304,000 participants from all fifty states, the District of Colombia, and Puerto Rico.

The CPS-3 Activity Validation Sub-study (CPS-3 AVSS) is a nested cohort of the CPS-3. In 2015, CPS-3 participants were stratified by sex and race/ethnicity and randomly selected to participate in the CPS-3 AVSS. Assuming an approximate 10% response rate, 10,000 CPS-3 participants were sent an invitation letter prompting them to pre-register and consent online. 750 participants were enrolled in the AVSS, and 713 participants with complete data will be included in the main validity and reliability analyses.

At the start of the CPS-3 AVSS, participants received a four-page pre-study survey which included two PA items, one sitting time item, and various demographic items. Subsequent data collection occurred over the following year, which was split into four equal quarters. During each of the four quarters, participants completed a seven-day diary, and on two non-consecutive quarters, participants wore accelerometers concurrent with the diaries. Approximately one year after completing the pre-study survey, participants completed the same four-page survey once again.

CPS-3 Measures

Seven-Day Diary: Participants completed one seven-day diary for each quarter of the study. Participants were asked to code their activities in 15-minute epochs throughout the day on seven consecutive days. Codes aligning with sedentary behaviors included: “sitting while eating, watching television, reading, driving, using computer/smartphone, etc.”, codes aligning with light physical activities included: “standing, very light activities, showering, dressing, etc.” and “walking (at a pace less than 3 mph), light activity, stretching, yoga, childcare, cooking, light yard work, household chores, light weightlifting, calisthenics”, and codes aligning with moderate-to-vigorous physical activities included: “walking (at pace of 3 to 3.9 mph), dancing, cycling (less than 10 mph), gardening, heavy yard word, mowing lawn, golfing without a cart” (moderate), “walking (at least 4 mph), recreational basketball, softball, baseball, hiking” (moderate), “cycling (10 to 13.9 mph), swimming, recreational sports (tennis, racquetball, soccer), aerobics, skiing, heavy weightlifting” (vigorous), “jogging (less than 6 mph), elliptical or stair climbing, competitive sports (basketball, flag football), boxing” (vigorous), and “vigorous lap swimming, running (at least 6 mph), cycling (14+ mph), intense manual work” (vigorous).

Daily hours of SED, LPA, MPA, VPA, and MVPA were calculated by summing the number of 15-minute epochs indicated at each intensity, multiplying by 15, and dividing by 60.

Days with fewer than 10 waking hours reported were considered invalid and excluded from the analysis. Daily average minutes of SED, LPA, MPA, VPA, and MVPA were calculated as a weighted average for quarters where a minimum of three valid days of data exists (‘valid’ quarters; n = 1 participant excluded for having 4 invalid quarters).

Accelerometer: During two non-consecutive quarters (Q1/Q3 or Q2/Q4), participants wore an Actigraph GT3x accelerometer on the hip aligning with the midline of the non-dominant thigh. Participants were instructed to wear the device for seven days concurrent with the seven-day diary during all waking hours, except when bathing or participating in water-based activities. Participants wearing the accelerometer exclusively outside the range of valid diary dates were excluded (n = 10).

Raw Actigraph data were processed using the Choi algorithm to calculate accelerometer wear time and the Sojourn algorithm to sum daily hours of sedentary, light, moderate, vigorous, and moderate-to-vigorous physical activity. Valid wear time was set using a minimum wear of 10 hours per day. Days failing to meet the minimum wear time were excluded from the analysis. Days where participants reported wearing the device to sleep were also excluded to avoid misclassifying sleep as sedentary time. Daily average minutes of SED, LPA, MPA, VPA, and MVPA were calculated as a weighted average for valid quarters (n = 15 participants excluded for 2 invalid quarters).

CPS-3 Survey: Participants repeated the same four-page pre-/post-validation survey at the end of the one-year validation study. Information on SED time was collected using the question, “During the past year, estimate the hours per day you spent on typical weekdays and weekends in each of the following activities. Please average your seasonal physical activities over the entire year. Try to account for all 24 hours per day”. SED time items included “sitting or lying down while watching TV” and “other sitting (at work, at computer, while driving, eating, etc.)”, with responses including “0, <1, 1-2, 3-4, 5-6, 7-8, 9-10, 11+ hours per day”. To generate a “total sitting time” value, the mean number of hours within the response categories (i.e. 0, 0.5, 1.5, 3.5, 5.5, etc. hours per day) were summed for the TV-related sedentary time and other sedentary time items.

Information on PA was collected using two questions. The abbreviated PA grid, “During the past year, estimate the hours per day you spent on typical weekdays and weekends in each of the following activities. Please average your seasonal physical activities over the entire year. Try to account for all 24 hours per day” included the brief responses: “standing or moving about” and “light activities” for LPA, as well as “weight lifting or resistance exercise” and “moderate activities” for MPA, and “strenuous activities” for VPA. An item for walking was also included on this question, but as pace could not be determined, walking was not included in the MVPA calculation. Responses to each activity item included “0, <1, 1-2, 3-4, 5-6, 7-8, 9-10, 11+” hours per day for the typical weekday and weekend day separately. The mean number of hours within the response categories (0, 0.5, 1.5, 3.5, 5.5, 7.5, 9.5, and 11 hours per day) were summed for each PA intensity level, and weighted averages for daily minutes of LPA, MPA, VPA, and MVPA were calculated.

The CPS-3 survey also included a more detailed PA grid: “During the past year, estimate how many hours per week and months per year you spent in each of the following activities: calisthenics (Pilates, sit-ups, pushups, etc.), yoga or Tai Chi, yard work or home maintenance (LPAs), lap swimming, aerobics class, elliptical or other aerobic machine, dancing, other aerobic recreation (golf without a cart, hiking, skiing, etc.), and weight training or resistance exercises (MPAs), jogging, running, tennis or racquetball, sports activities (VPAs), and walking”. The question “What is your usual walking pace outdoors” was used to determine the intensity of walking for the detailed PA questionnaire. Walking by participants selecting “easy, causal (less than 2mph)” was classified as LPA, while walking by participants selecting “normal, average (2-2.9mph)”, “brisk pace (3-3.9mph)”, or “very brisk/striding (4mph or faster)” was classified as MVPA. Responses to each individual activity included: “none, <1, 1-2, 3, 4-6, 7+” hours per week and “1-3, 4-6, 7-9, 10-12” months per year. The mean number of hours within the response categories (0, 0.5, 1.5, 3, 5, and 7 hours per day) were summed for each PA intensity level, and multiplied by the proportion of the year active (0.25, 0.5, 0.75, 1) to generate average daily minutes spent at each PA intensity. Participants missing pre- or post-survey PA or SED time information were excluded (n = 12).

2.3. The Method of Triads

Criterion validity and one-year test-retest reliability of the PA and SED measures were assessed via the method of triads. Based on factor analysis theory, the method of triads assumes that the existence of linear relationships among the seven-day diary, accelerometer, and post-validation survey will imply that the three methods will also be related to the ‘true’ latent (unobserved) exposure.(26, 27)

This methodology encompasses calculating three validity coefficients, which are the correlations between the ‘true’ time spent at each activity level (sedentary, light, moderate, vigorous, and moderate-to-vigorous) and the measured time spent at each activity level, from a set of three pairwise correlations among activity measured by accelerometry, the seven-day diary, and the post-validation survey.

Validity coefficients (VC) were calculated with the following formulas:

$$VC_{AT} = \sqrt{r_{AD} * r_{AS} / r_{DS}}$$
$$VC_{DT} = \sqrt{r_{AD} * r_{DS} / r_{AS}}$$
$$\boldsymbol{VC_{ST} = \sqrt{r_{AS} * r_{DS} / r_{AD}}}$$

Where VC_{AT}, VC_{DT}, and VC_{ST} are the validity coefficients between the 'true' time spent at each activity level and the accelerometer-measured, diary estimated, and survey estimated time at each activity level, respectively. Bootstrap 95% confidence intervals were calculated so the three VCs can be compared.(25) The method of triads was also used to calculate criterion validity estimates and bootstrap 95% confidence intervals stratified by age, BMI, educational attainment, occupational status, and adherence to the 2008 physical activity guidelines for Americans (based on accelerometer data).

Reliability of specific survey items was assessed by calculating Spearman correlation coefficients (ρ) between the pre- and post-survey responses for each individual item (e.g., 'weight lifting or resistance exercises'). Reliability estimates were also calculated stratified by age, BMI, educational attainment, occupational status, and adherence to physical activity guidelines (based on accelerometer data). A sensitivity analysis was conducted restricting to participants with seven valid days of diary data and seven valid days of accelerometer data defined using a 14-hour wear time minimum.

2.4. Physical Activity, Sedentary Time, and Health

Research suggests that MVPA may lower the risk of developing or dying from chronic diseases such as cardiovascular disease, type 2 diabetes mellitus, stroke, and some cancers (35-39). The 2008 physical activity guidelines for Americans (40-42) state that adults should engage in at least 150 minutes of moderate (such as walking at a pace of 20 minutes per mile or 3 miles per hour) or 75 minutes of vigorous-intensity (such as running, swimming, or biking) physical activity per week to achieve health benefits. However, nearly half of all adults in the United States do not regularly engage in recommended levels of PA.

Distinct from physical inactivity, the amount of time spent sedentary has increased significantly over the past few decades. This increase in SED, characterized by very low energy expenditure (≤1.5 METs) while in a sitting, reclining, or lying position (43), is largely attributed to technologic advancements, increased dependence on automobiles for transportation, and engagement in more sedentary activities during leisure time (e.g. screen-based entertainment). Recent evidence suggests that excess time spent SED may be associated with deleterious health effects independent of physical inactivity. (44-47). For example, a recent meta-analysis including over one million participants reported a 34% higher all-cause mortality risk for adults sitting 10 hours per day (vs. 0-3 hours/day), even after adjusting for MVPA. (45)

Most existing studies explore the associations of SED time and various health outcomes without considering the physical activities being displaced or the limit of time. This has left a gap in our understanding of healthful proportions of activity time, as it is not yet entirely clear if it is considerably more beneficial to replace sedentary time with MVPA, or if it is similarly beneficial to replace sedentary time with LPA. ISMs estimate the effect of replacing sedentary time with time-matched physical activities. By assuming there is a fixed amount of time available in a day, the ISM allows for the consideration of activities displaced within available discretionary time.(19, 20)

The ISM was implemented in this study to estimate the time-substitution associations of replacing thirty minutes of daily leisure-time sitting with equivalent amounts of various intensities of PA and mortality risk in the Cancer Prevention Study-II Nutrition Cohort.

2.5. Cancer Prevention Study-II

The Cancer Prevention Study-II (CPS-II) is a prospective study of cancer mortality initiated by the American Cancer Society in 1982, and includes approximately 1.2 million participants. In 1992, roughly half of the CPS-II participants were randomly selected to join the CPS-II Nutrition Cohort (CPS-II NC), a nested cohort of the CPS-II. The CPS-II NC, which includes over 184,000 participants, was established to obtain information on additional health behaviors, including diet patterns, PA, and sitting time. CPS-II NC participants were between the ages of 50 and 74 at enrollment.

CPS-II NC participants completed a 10-page questionnaire at enrollment, and subsequent questionnaires were mailed every two years beginning in 1997 to update exposure information and ascertain newly diagnosed medical problems. The response rate among participants for each follow-up survey was at least 88%. The 1999 survey was used as the baseline for this analysis, as it included detailed questions on PA and SED.

Time spent sitting was assessed with the question, "During the past year, what was your average total time per week spent at each of the following activities?" with responses including: sitting at work, sitting or driving in a car/bus/train, sitting or lying watching TV, sitting at home reading, and other sitting. Responses to each individual activity included: none, 1-39 min, 40-89 min, 1.5 hrs, 2-3 hrs, 4-6 hrs, 7-10 hrs, 11-20 hrs, 21-30 hrs, 31-40 hrs, 40+ hrs The midpoint value from each sitting category was summed and used to generate average daily total sitting time.

Information on physical activity was collected with the question, "During the past year, what was your average total time per week spent at each of the following activities?". Time spent dancing, gardening/mowing/planting, and doing low intensity exercise will be used to generate a daily “light intensity physical activities” variable. Similarly, time spent jogging/running, lap swimming, tennis or racquetball, bicycling/exercise machines, and engaging in aerobics/calisthenics will encompass the daily “moderate-to-vigorous intensity activities” variable. The midpoint values from responses including: none, 1-19 min, 20-59 min, 1 hr, 1-1.5 hrs, 2-3 hrs, 4-6 hrs, 7-10 hrs, and 11+ hrs, were used to form average daily LPA and MVPA values.

One potential limitation of the 1999 CPS-II NC survey is the lack of information on certain activities of daily living (ADLs), such as cleaning, self-care, cooking, or child/older adult care. As these ADLs are particularly common for older adults, LPA time may be underestimated in this analysis.

The primary outcome was death, which was ascertained through biennial linkage of the cohort with the National Death Index. (48) Causes of death were classified with the *International Classification of Diseases* (ICD), the Tenth Revision for deaths occurring one year after the 1999 survey completion through 2014. Cancer, cardiovascular disease, other causes, and all-cause mortality risks associated with isotemporal replacement of sitting time was assessed.

2.6. Isotemporal Substitution Model

Isotemporal substitution models estimate the effect of replacing sedentary time with time-matched physical activities. By assuming there is a fixed amount of time available in a day, ISM allow for the consideration of activities displaced by PA or SED time. This model estimates the association of the activity of interest (e.g., sedentary time) as well as the activity being replaced (e.g. LPA or MVPA) while holding total time and the influence of other activities in the model constant.

Cox proportional hazards regression models and 95% confidence intervals were calculated for the isotemporal substitution of thirty minutes of sitting time LPA or MVPA in three models: 1) adjusted for age and sex, 2) adjusted for age, sex, and other potential confounding factors, and 3) adjusted for age, sex, confounding factors, and BMI. Additional potential confounders included: race (white, black, other/unknown), alcohol use (non-drinker, <1, 1, ≥2 drinks/day), smoking status (never, current, former, unknown), years since quitting among former smokers (<10, 10-19, ≥ 20 years), cigarette frequency and smoking duration among current smokers (<20 cigarettes/day and smoking ≤35 years, <20 cigarettes/day and smoking >35 years, 20+ cigarettes/day and smoking ≤35 years, 20+ cigarettes/day and smoking >35 years), aspirin use (non-user, <15, 15-29, 30+ pills/month), education (high school or some college, college graduate or higher, unknown), occupational status (employed, not employed/retired, unknown), ACS dietary guidelines adherence score (0-<3, 3-<6, ≥6), and comorbidity score (0, 1, ≥2 comorbidities, including high blood pressure, diabetes, and high cholesterol).

The ISM used in the proposed main analysis can be expressed as:

$$\text{Mortality risk}_{\text{sitting}} = (b_1)\text{ light physical activity time} + (b_2)\text{ moderate-to-vigorous intensity activity time} + (b_3)\text{ total duration} + (b_4)\text{ covariates,}$$

where $b_1 – b_4$ are coefficients of activities or covariates and 'total duration' is the sum of the average daily duration reported for each of the sedentary and active behaviors. When one behavior (in the case of the model above, sitting time) is eliminated, the total duration coefficient represents the omitted activity component, and the remaining coefficients represent the consequence of substituting thirty minutes of that activity for the eliminated activity while holding all other activities constant.

Secondary analyses tested for effect modification of the mortality benefits associated with the isotemporal replacement of sedentary time by sex, age group, and BMI group. Several sensitivity analyses were also conducted: 1) among participants who were life-long non-smokers or former smokers of more than 20 years at baseline (n = 81,268), 2) among participants without physical limitations (n = 101,136), and 3) excluding deaths occurring within the first two years of follow-up to address the possibility of reverse causality (n = 100,751). Interaction terms between sitting time and follow-up time were created to test the Cox proportional hazards assumption. All statistical tests were two-sided and $p<0.05$ was considered statistically significant. Analyses were conducted using SAS v.9.4 (SAS Institute Inc., Cary, NC).

The isotemporal substitution technique has grown in popularity over the last few years. While many early isotemporal substitution studies primarily used cross-sectional data to explore associations between replacing sedentary time and various metabolic outcomes, more recently, there have been a few prospective studies exploring the associations between the replacement of sedentary time and mortality risk.(49-51) One prospective study found significant reductions in all-cause mortality risk for substituting one hour of sitting time with one hour of walking (Hazard Ratio (HR), 95% Confidence Intervals = 0.86, 0.81-0.90) or with one hour of MVPA (HR = 0.88, 0.85-0.90).(52) Another study found meaningful differences in substitution effects based on participants' current level of activity.(53) For more active participants (those reporting ≥2 hours/day of total physical activity [LPA and MVPA combined]), the substitution of one hour/day of sedentary time was associated with a reduced risk for all-cause mortality when replaced with equal amounts of MVPA (HR = 0.91, 0.88-0.94]), but there were no benefits associated with replacing one hour/day of sedentary time with one hour/day of non-exercise activity (HR = 1.0, 0.98-1.02). On the other hand, the less active participants benefited from replacing one hour/day of sedentary time with one hour/day of non-exercise physical activity (HR = 0.70, 0.66-0.74), although mortality benefits were greater when sedentary time was replaced with MVPA (HR = 0.58, 0.54-0.63).

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CHAPTER 3

DEMOGRAPHIC-SPECIFIC VALIDITY OF THE CANCER PREVENTION STUDY-3 SEDENTARY TIME SURVEY[1]

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[1] Rees-Punia E, Matthews CE, Evans EM, Keadle SK, Anderson RL, Gay JL, Schmidt MD, Gapstur SM, Patel AV. Submitted to *Medicine and Science in Sports and Exercise*, 2/7/18.

3.1. Abstract

PURPOSE: This study examined the one-year test-re-test reliability and criterion validity of sedentary time survey items in a subset of participants from a large, nationwide prospective cohort.

METHODS: Participants included 423 women and 290 men aged 31-72 years in the Cancer Prevention Study-3 (CPS-3). Reliability was assessed by computing Spearman correlation coefficients between responses from pre- and post-study surveys. Validity was assessed by comparing survey-estimated sedentary time with a latent variable representing true sedentary time estimated from the seven-day diaries, accelerometry, and surveys through the method of triads. Sensitivity analyses were restricted to 566 participants with an average of 14+ hours of diary and accelerometer data per day for seven days per quarter.

RESULTS: Reliability estimates for total sitting time were strong across all demographic strata (Spearman $\rho \geq 0.6$), with significant differences by race ($p=0.01$). Reliability estimates were strongest for the TV-related sedentary time item (Spearman $\rho=0.74$, 95% CI: 0.70, 0.77). The overall validity coefficient (VC) for survey-assessed total sedentary time was 0.62 (95% CI: 0.55, 0.69), although VCs varied by age group and activity level ($p<0.05$). However, VCs were similar across groups ($p<0.05$) when restricting to highly compliant participants in a sensitivity analysis.

CONCLUSION: The CPS-3 sedentary behavior questionnaire has acceptable reliability and validity for ranking or categorizing participants according to sedentary time. Acceptable reliability and validity estimates persist across various demographic sub-groups.

3.2. Introduction

Much of the evidence for the independent association of sedentary behavior, waking behavior characterized by very low energy expenditure while in a sitting or lying posture, with chronic disease and premature mortality comes from large prospective epidemiological studies.(1-6) For practical reasons regarding costs, as well as participant and researcher burden, many epidemiological studies have relied on self-reported measures of sedentary behavior.(7) While subjective measures remain the most feasible option for large-scale studies, their use may be limited by participant comprehension, difficulty recalling events, or other sources of random and systematic error.(8) To assess and potentially limit the influence of such issues, studies must be conducted to evaluate the validity and reliability of a measure.(9) Valid and reliable measures are necessary for accurately and consistently describing an exposure, and for understanding the presence and strength of associations observed in epidemiologic studies.

Existing self-reported measures of sedentary time vary greatly in the time frame queried, domains assessed, and metrics evaluated. Evidence suggests that sedentary time may be better assessed through a composite score, obtained by summing sedentary time in different domains (such as television viewing, travel, or work-related sitting), as opposed to single item surveys which tend to have lower validity.(10) However, prior studies have demonstrated that the most commonly used composite sedentary behavior questionnaires vary widely in both reliability (Spearman test-retest ρ = 0.28-0.93) and validity estimates (Spearman ρ = 0.14-0.49 compared with accelerometry; Spearman ρ = 0.60-0.75 compared with activity log) of self-reported sedentary time.(10, 11) Further, questionnaires that appear to be valid in one population are not necessarily valid in others. Not surprisingly, validity estimates can vary significantly across sub-groups, including sex, race/ethnicity, age, body mass index (BMI), and education level.(7, 10)

As sedentary behaviors are complex and multi-dimensional, evaluating measure reliability and validity remains a challenge. Primarily, validation studies may be limited by the scarcity of simple gold standard criterion measures for free-living sedentary behavior. Direct observation is a valid criterion for measuring sedentary time; however, this method is labor-intensive and requires the skill and time of highly trained researchers, making it less feasible for studies large enough to detect differences in validity among various sub-groups.(12) While accelerometers are appropriate for measuring the velocity of ambulatory bodily movements, they do not aptly measure posture or non-ambulatory activities. Furthermore, they often produce results that are highly influenced by data processing and proper wear.(13, 14) Accelerometer/Inclinometer devices, such as the ActivPAL, are accurate for measuring posture (i.e., sitting vs. standing), but may be prone to misclassifying some seated physical activities (such as resistance training or rowing) as sedentary time.(15)

Additionally, measurement error associated with accelerometers, diaries, and recall surveys may be correlated. This can be problematic as traditional validation approaches (for example, correlations between two measures) technically require independent measurement error between the two measures.(16) The addition of a third measure can minimize this limitation when linear relationships between a latent ‘true’ sedentary time measure and the amount measured by three independent instruments are assumed; this methodology is referred to as the method of triads.(16-19) Although the method of triads is not yet commonly used in sedentary or physical activity survey validation studies, it has been used extensively in nutritional epidemiology and psychology validation studies and can realistically be applied in the validation of any continuous exposure measure.(20-25)

The present study sought to examine the one-year test-retest reliability and criterion validity of sedentary time survey items in a subset of participants from a large, nationwide prospective cohort study of U.S. adults. Results from this study will help inform survey design and/or survey selection decisions for future epidemiologic studies of sedentary behavior. Secondarily, this study aimed to evaluate the reliability and validity estimates of the sedentary time survey items stratified by sex, race/ethnicity, age, body mass index (BMI), educational attainment, occupational status, and adherence to U.S. federal physical activity guidelines (based on accelerometer data).

3.3. Methods

Study Population

The Cancer Prevention Study-3 (CPS-3) is a prospective study of cancer incidence and mortality initiated by the American Cancer Society (ACS).(26) Participants were recruited at ACS fundraising events or community enrollment drives between 2006 and 2013. Over 304,000 participants aged 30 to 65 years with no history of cancer (except for basal or squamous cell skin cancer) were enrolled. CPS-3 participants completed a baseline survey at enrollment, and are sent repeat surveys every three years to update exposure information.

In 2015, CPS-3 participants were stratified by sex and race/ethnicity and randomly invited to participate in the CPS-3 Activity Validation Sub-study (CPS-3 AVSS). Among the 10,000 participants invited, 1,801 participants pre-registered and consented to participate in the AVSS, and the first 300 white women, 150 white men, 150 Latino/as, and 150 African American/Black participants to complete the 2015 CPS-3 follow-up survey were enrolled into the AVSS. In total, 751 participants were enrolled in the CPS-3 AVSS. The CPS-3 and CPS-3 AVSS are approved by the Institutional Review Board at Emory University.

AVSS Participants were sequentially excluded from the current analyses for the following reasons: having four quarters of invalid diary data (n = 1), lacking sufficient accelerometer wear (≥4 days, ≥10 hours/day wear time) within the range of valid diary dates (n = 25), or missing pre- or post-survey sitting time information (n = 12).

Study Design

At the start of the CPS-3 AVSS, participants received a four-page ‘pre-study survey’ which included sitting time, physical activity, and various demographic items. Subsequent data collection occurred over the following year, which was split into four equal quarters (Figure 3.1). During each of the four quarters, participants completed a seven-day diary, and during two non-consecutive quarters, participants wore accelerometers concurrent with diaries. Approximately one year after completing the pre-study survey, participants completed the same four-page survey once again (the ‘post-study survey’). Participants could receive a maximum incentive of $100 upon completion of the AVSS, with deductions for incomplete diaries ($20) or lost accelerometers ($25).

Measures

Seven-Day Diary: Participants completed one seven-day diary for each quarter of the study, during which they were asked to code their activities in 15-minute epochs throughout the entire day on seven consecutive days. Codes aligning with sedentary behaviors included: “sitting while: eating, watching television, reading, driving, using computer/smartphone, etc.”. Days with fewer than 10 waking hours reported were considered invalid and excluded from the analysis. Daily average minutes of sedentary time was calculated as a weighted average for quarters with a minimum of four valid days. Quarterly values were further averaged to generate mean daily minutes of sedentary time which account for seasonal changes in behavior.

Accelerometer: During two non-consecutive quarters (Q1/Q3 or Q2/Q4), participants wore an Actigraph GT3x accelerometer on the hip aligning with the midline of the non-dominant thigh. Participants were instructed to wear the device for seven consecutive days concurrent with the seven-day diary during all waking hours, except when bathing or participating in water-based activities. Accelerometer data that was recorded on invalid diary dates were excluded to maintain an overlap in valid accelerometer/diary days.

Raw Actigraph data were processed using the Choi algorithm to calculate accelerometer wear time and the sojourn-3 axis algorithm to estimate daily sedentary time.(27-30) The sojourn-3 axis method is a hybrid machine-learning, neural network, and decision tree analysis algorithm which uses second-by-second triaxial accelerometer counts to estimate free-living sedentary time.(29) Days failing to meet the wear time minimum of 10 hours/day were excluded from the analysis. Daily average minutes of sedentary time was calculated as a weighted average for quarters with a minimum of four valid days.(31) Quarterly values were further averaged to generate mean daily minutes of sedentary time which account for seasonal changes in behavior.

Survey: Participants completed the same four-page survey at the beginning and end of the one-year validation study. Information on sedentary time was collected using the question, “During the past year, estimate the hours per day you spent on typical weekdays and weekends in each of the following activities. Please average your seasonal physical activities over the entire year. Try to account for all 24 hours per day”. Sedentary time items included “sitting or lying down while watching TV" and "other sitting (at work, at computer, while driving, eating, etc.)", with responses including "0, <1, 1-2, 3-4, 5-6, 7-8, 9-10, 11+ hours per day". To generate a "total sitting time" value, the mean number of hours within the response categories (i.e. 0, 0.5, 1.5, 3.5, 5.5, etc. hours per day) were summed for the TV-related sedentary time and other sedentary time items.

Statistical Analysis

Reliability of specific survey items was assessed by calculating Spearman correlation coefficients (ρ) between the pre- and post-survey responses for each individual item. Reliability estimates were also calculated stratified by age group, BMI (18-24.9 kg/m^2 normal, 25-29.9 kg/m^2 overweight, ≥30 kg/m^2 obese), educational attainment, occupational status, and adherence to physical activity guidelines (based on accelerometer data). Differences among subgroups were tested for statistical significance using Fisher's *z* test.

Criterion validity of the sitting measure was assessed via the method of triads. Based on factor analysis theory, the method of triads can be used to estimate model parameters which define the theoretical relationship between three measured exposures and the 'true' latent (unobserved) exposure.(16, 18) This methodology encompasses calculating three validity coefficients (VC), which are correlations between the 'true' time spent sedentary and the measured time spent sedentary. VCs are calculated using a set of three pairwise correlation coefficients (Pearson *r*) among the accelerometer, the seven-day diary, and the post-study survey in the following formulas:

$$VC_{AT} = \sqrt{r_{AD} * r_{AS} \,/\, r_{DS}}$$

$$VC_{DT} = \sqrt{r_{AD} * r_{DS} \,/\, r_{AS}}$$

$$VC_{ST} = \sqrt{r_{AS} * r_{DS} / r_{AD}}$$

Where A, D, and S are the measurements from the accelerometer, diary, and survey, respectively, and VC_{AT}, VC_{DT}, and VC_{ST} are the validity coefficients between the 'true' time spent sedentary and the accelerometer-measured, diary estimated, and post-study survey estimated sedentary time, respectively. Bootstrapping methods were used to calculate 95% confidence intervals.(17) The method of triads was also used to calculate criterion validity estimates and bootstrap 95% confidence intervals stratified by age, BMI, educational attainment, occupational status, and adherence to the 2008 U.S. federal physical activity guidelines (based on accelerometer data). A sensitivity analysis was conducted restricting to participants with seven valid days of diary data and seven valid days of accelerometer data defined using a 14-hour wear time minimum (n=566).

3.4. Results

Overall, 423 women and 290 men with a mean age of 51.7 (range 31-72) years were included in these analyses. Baseline characteristics are shown in Table 3.1. Participants recorded diary data for an average of 6.7 days per quarter and 16.8 waking hours per day, and wore the accelerometers for an average of 6.6 days per quarter for 16.1 hours per day. Overall, participants reported an average of 1.8 fewer hours of sitting time on the post-study survey compared to the diary, while accelerometer-measured sitting time comported well with the diary-measured sitting time (average difference of 22 min).

The correlations for rank-order agreement of total sitting time between baseline and one-year retest surveys were moderate or strong (≥0.55; Table 3.2). Significant differences in reliability estimates were seen across racial/ethnic groups, where Latino/a participants had significantly lower reliability estimates compared to non-Latino/a white participants. Test-retest correlations for total sitting were otherwise similar according to sex, BMI, education, employment status, age, and PA guideline adherence.

As shown in Table 3.2, test-retest correlations varied by domain-specific item, although reliability estimates were generally strong for both sitting items and all demographic strata (≥0.6). The Spearman correlations were generally stronger for the “sitting or lying down while watching TV” item, where the strongest correlations were seen among overweight (0.75, 95% CI: 0.68, 0.79) and age 60+ (0.79, 95% CI: 0.74, 0.84) sub-groups. Additionally, a pattern of increasing reliability by age was observed for the TV viewing item. For the “other” sitting item, which included work, eating, and driving, significant differences were seen across racial/ethnic groups, with lower reliability estimates among Latino/a participants compared to non-Latino/a black and white participants. Representing the most drastic difference in other sitting time among strata, reliability estimates were higher among employed participants (0.70, 95% CI: 0.65, 0.74) compared to participants not employed during data collection (0.39, 95% CI: 0.24, 0.52).

Demographic-specific Pearson bivariate correlations between the accelerometer-, diary-, and survey-measured total sitting time are presented in Table 3.3. The overall correlation for agreement of total sitting time between the survey and diary was 0.53 (0.47, 0.58), although there were significant differences by age group. Agreement between the survey and accelerometer was slightly lower (0.41, 95% CI: 0.35, 0.47).

VCs for survey-assessed total daily sitting time are presented in Table 3.4. Among the entire sample, the VC between survey-assessed sitting time and the latent sitting time variable was 0.62 (95% CI: 0.55, 0.69). However, among the various demographic strata, VCs ranged from 0.51 ((95% CI: 0.33, 0.68; for participants not currently employed) to 0.75 ((95% CI: 0.63, 0.88; for participants between the ages of 30-39). Significant differences were seen among the youngest and oldest age groups, although there was no clear pattern by age. VCs also differed by physical activity guideline compliance, such that participants meeting guidelines had a significantly higher VC. Differences across all other demographic groups were statistically insignificant.

Over 79% of participants (n = 566) had complete diary and accelerometer data (seven valid days of data/quarter using a 14-hour wear time minimum) and were included in the sensitivity analysis (Table 3.5). Overall, most VCs did not change significantly, although there was a small increase in validity estimates among participants aged 40-49 years and a decrease among participants with obesity. There were differences in the percent of participants included in the sensitivity analysis by strata. For example, 85.5% of normal weight participants and 83.3% of white participants had complete enough accelerometer/diary data for inclusion in this analysis; meanwhile, 66.9% of obese participants and 66.9% of black participants were included. All differences among strata were attenuated and no longer statistically significant when restricting to participants with complete data.

3.5. Discussion

As evidence of the adverse effects of a sedentary lifestyle accumulates, it is important to assure that this exposure is appropriately measured. Validation studies of self-reported measures of sedentary time are less common than validation studies of self-reported measures of physical activity, partially because of the relatively novel understanding of excess sedentary time, but also because of the costs, time, and burden associated with many objective sitting time measures. In the current study, we used the method of triads with accelerometer and seven-day diary data to model ‘true’ sitting time for comparison with survey-measured sitting time.

The CPS-3 sitting time survey had moderate or strong reliability across all sub-groups, with rank-order correlations comparable to prior studies of commonly used sitting time surveys.(32, 33) However, stronger reliability was generally observed for the TV sitting item compared to the “other sitting” item. This finding was expected as prior studies have suggested that items regarding sedentary behaviors that are done on a regular basis and for prolonged periods of time, such as watching TV, tend to exhibit stronger reliability than behaviors done less regularly (including driving and ‘other’ general sitting activities).(10) This theory may also help explain the linear trend for reliability estimates by age group for TV sitting, as adults tend to watch more TV as they age, with the largest increase in TV viewing time occurring around the retirement transitional period.(34, 35) Further, it may be easier to recall time spent sitting while watching TV in general, as TV shows tend to follow a certain time structure (i.e., 30 or 60 minute-long shows) which can feasibly be summed. The largest difference between strata was seen for reliability of the “other sitting” item by employment status, where stronger reliability was observed for employed participants (0.70 for employed vs. 0.39 for not currently employed). The difference by employment status for “other sitting”, which includes sitting for work, may be due to the long test-retest period. As the employment status question asks participants if they were “employed in the past year”, and 6.5% of participants changed their employment status during the one-year data collection period, there may have been a true change in the time spent sitting for work between the pre- and post- survey periods for these participants. Further, it is possible that participants who are employed full time have more consistent schedules and sitting patterns and can therefore report sitting time more reliably.

It is important to note that the average number of minutes/day spent sitting estimated from the CPS-3 survey was considerably lower than the number of minutes/day spent sitting according to the accelerometer or seven-day diary data. These results are consistent with prior reviews, which suggest that questionnaires tend to underestimate sitting time and rarely exhibit good validity.(36) Correlations for total sitting time measured by CPS-3 and accelerometry reported in the current study were similar or slightly higher (0.41 (0.35, 0.47)) than those for other surveys. A large systematic review of the criterion (accelerometer) validity of several sedentary time surveys, for example, reported a median Spearman correlation coefficient of 0.23.(36) A more recent validity study of the England Physical Activity and Sedentary Behavior Assessment Questionnaire (PASBAQ), which parallels the CPS-3 in format and verbiage although it assesses activity during a different time frame, reported Spearman correlations of 0.31 (0.25, 0.37) for women and 0.25 (0.19, 0.31) for men.(37) Further evidence of the acceptable validity of the CPS-3 survey for assessing sitting time is demonstrated by the overall VC of 0.62 (95% CI: 0.55, 0.69). However, the magnitude of VCs did differ between sub-groups. The largest difference was observed between the youngest (age 30-39 years) and oldest (age 60+ years) participants, but statistically significant differences were also observed between participants adhering to PA guidelines and their non-adhering counterparts. These differences may be partially explained by the idea that participants with less structured lives (lacking a consistent work or exercise schedule) may have a more difficult time accurately recalling their behaviors. Together, these results suggest that the CPS-3 survey is suitable for ranking or classifying participants according to levels of sedentary time, but may not be suitable for detecting small changes in sedentary time.

Restricting to participants with complete data (seven valid days of diary and accelerometer data defined by a 14-hour wear time minimum) increased the overall VC, although not significantly. Perhaps just as interesting was the difference in compliance (i.e., the percent of original sample included in the sensitivity analysis) across sub-groups. Given the stark contrasts seen among race/ethnicity and BMI categories, it is important to understand why it may be more difficult for some sub-groups to comply to longer accelerometer wear/diary completion protocols. For example, it is possible that participants with excess abdominal adiposity, particularly women, may feel more discomfort or embarrassment with hip-mounted accelerometer wear, and therefore may be less willing to wear the device for longer periods of time.(38) Participants with obesity also tend to over-report physical activity and under-report sedentary time, which may have further contributed to the weaker VC among obese participants in the sensitivity analysis.(39) Overall, sensitivity analysis results suggest that the CPS-3 measure is appropriate for use among participants with diverse demographic characteristics, as there were no statistically significant differences in validity by sub-group.

This study has several strengths, including a large, demographically diverse sample size with the power to detect differences among sub-groups. Participants in this study were highly compliant, as evidenced by both the high retention rate throughout the year-long data collection process and the high proportion of participants with complete data (~79%), even when using a 14-hour wear time minimum. This study is also strengthened by the attempts to capture seasonal variation in sitting behaviors through quarterly data collection. Additionally, modeling a latent variable representing the ‘true’ amount of sitting time, based on seven-day diary and objective accelerometer data, allowed for the evaluation of validity in a large cohort without the use of direct observation or activPAL devices.

This study also has several limitations that ought to be considered. Although participant compliance is a strength, it is possible that the CPS-3 AVSS participants are not representative of the underlying CPS-3 population. As the participants in this study were seemingly invested, they may have spent more time and effort on survey responses than the average respondent. Participants may have also been motivated by the monetary incentive, although it is important to note that 18% of participants donated their study incentive to the ACS. Another potential limitation of this study is the very long test-retest period. As the CPS-3 survey asks participants to report their daily average sitting time during the past year, it is not possible to determine if changes in one-year responses are due to true changes in sitting time or poor reliability. Despite the long test-retest period in the current study, studies with much shorter retest periods produced reliability estimates of similar magnitude.(32, 33) Further, as with any study reliant on accelerometer data, the lack of agreement regarding cut-points for sedentary time and the various other processing decisions may influence results.(40) However, efforts were made to select algorithms which have been shown to provide optimal data when used in combination with a self-reported wear log.(41) And finally, the CPS-3 sitting time items do not allow for the identification of breaks in sedentary time or very long bouts of sedentary time, which may be particularly important metrics of sedentary time.

Conclusion

The CPS-3 sedentary behavior questionnaire has acceptable reliability and validity for ranking or categorizing participants according to sedentary behavior level. The current findings further suggest that participant responses are not systematically biased by sex, age, race/ethnicity, BMI, education, occupational status, or current physical activity level.

3.6. References

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Table 3.1 Baseline characteristics of the Activity Validation Sub-study (N = 713)

	N (%) or Mean ± SD	Mean daily sitting time-survey (min)	Mean daily sitting time-diary (min)	Mean daily sitting time-accel. (min)
All	713	450.7 ± 173.2	557.3 ± 135.3	579.7 ± 96.7
Demographic Characteristics				
Sex				
Women	423 (59.3%)	453.7 ± 180.4	540.8 ± 126.7	567.5 ± 95.5
Men	290 (40.7%)	446.2 ± 162.2	581.3 ± 144.0	597.4 ± 95.9
Race/Ethnicity				
Black	136 (19.0%)	503.0 ± 194.3	581.8 ± 145.9	600.3 ± 89.1
White	469 (65.8%)	436.7 ± 165.8	553.8 ± 132.6	577.9 ± 96.0
Latino/a	108 (15.2%)	445.1 ± 165.3	541.5 ± 130.8	561.4 ± 105.0
Age group				
30-39 years	97 (13.5%)	448.8 ± 175.1	548.5 ± 127.6	582.0 ± 98.5
40-49 years	167 (23.5%)	459.1 ± 175.7	551.0 ± 140.9	583.5 ± 99.9
50-59 years	219 (30.8%)	458.1 ± 169.3	547.8 ± 135.1	575.8 ± 92.2
60+ years	230 (32.3%)	438.2 ± 174.6	575.2 ± 133.8	579.7 ± 98.5
BMI (kg/m^2)				
Underweight	7 (1.0%)	412.8 ± 165.1	565.1 ± 158.4	622.2 ± 122.8
Normal weight	282 (39.7%)	420.7 ± 159.0	530.6 ± 126.8	560.7 ± 97.2
Overweight	249 (35.1%)	440.2 ± 460.5	576.2 ± 138.5	584.3 ± 97.0
Obese class I	112 (15.8%)	485.3 ± 176.2	583.0 ± 140.2	599.8 ± 94.0
Obese class II	60 (8.5%)	576.2 ± 213.2	557.3 ± 128.0	605.1 ± 80.7
Missing	3 (0.4%)	460.0 ± 348.1	515.4 ± 221.2	618.1 ± 33.5
Education				
HS/some college	182 (25.5%)	474.9 ± 205.5	544.2 ± 129.3	563.6 ± 95.5
College grad	530 (74.4%)	442.7 ± 160.0	562.0 ± 137.2	585.6 ± 96.3
Missing	1 (0.1%)	257.4 ± 0.0	405.5 ± 0.0	376.3 ± 0.0
Employment				
Employed	574 (81.3%)	460.2 ± 164.2	562.3 ± 135.1	584.5 ± 95.1
Not employed	132 (18.7%)	411.6 ± 204.5	540.4 ± 136.0	557.7 ± 102.5
Missing	7 (1.0%)	401.1 ± 161.2	464.5 ± 87.1	593.0 ± 55.3
PA guidelines*				
Meets	279 (39.1%)	418.8 ± 160.1	546.2 ± 135.4	564.1 ± 91.0
Does not meet	434 (60.9%)	469.8 ± 180.0	568.2 ± 132.6	588.0 ± 99.1
Avg. daily accel. wear time (min)	963.3 ± 165.5	-	-	-
Avg. daily diary waking time (min)	1009.9 ± 115.1	-	-	-

*U.S. Federal Physical Activity Guideline adherence defined using accelerometer MVPA bout data

Table 3.2 Estimates of reliability for pre- and post-survey sitting items, Spearman ρ

	Total Sitting ρ (95% CI)[a]	***p* value****	**TV Sitting ρ (95% CI)**	***p* value****	**Other Sitting ρ (95% CI)**	***p* value****
All	0.67 (0.63, 0.71)		0.74 (0.70, 0.77)		0.71 (0.67, 0.74)	
Sex		0.73		0.72		0.96
Women	0.68 (0.62, 0.73)		0.74 (0.70, 0.78)		0.71 (0.66, 0.75)	
Men	0.67 (0.60, 0.72)		0.73 (0.67, 0.78)		0.71 (0.65, 0.76)	
Race/Ethnicity		**0.01**[1]; 0.18[2]; 0.28[3]		0.68[1]; 0.07[2]; 0.30[3]		**0.03**[1]; 0.18[2]; 0.41[3]
Black	0.64 (0.52, 0.73)		0.66 (0.55, 0.74)		0.68 (0.57, 0.76)	
White	0.71 (0.66, 0.75)*		0.75 (0.71, 0.78)		0.74 (0.70, 0.78)*	
Latino/a	0.55 (0.39, 0.66)*		0.73 (0.62, 0.80)		0.61 (0.48, 0.72)*	
BMI (kg/m^2)		0.69[4]; 0.63[5]; 0.23[6]		0.76[4]; **0.03**[5]; **0.02**[6]		0.63[4]; 0.26[5]; 0.16[6]
Normal weight	0.66 (0.59, 0.72)		0.73 (0.67, 0.78)*		0.62 (0.63, 0.75)	
Overweight	0.64 (0.56, 0.71)		0.75 (0.68, 0.79)*		0.71 (0.65, 0.77)	
Obese	0.66 (0.56, 0.73)		0.64 (0.55, 0.72)*		0.73 (0.66, 0.79)	
Education		0.91		0.65		0.23
HS/some college	0.67 (0.58, 0.75)		0.71 (0.63, 0.77)		0.67 (0.58, 0.74)	
College grad	0.67 (0.62, 0.72)		0.74 (0.69, 0.77)		0.72 (0.68, 0.76)	
Employment		0.29		0.28		**<0.001**
Employed	0.67 (0.63, 0.72)		0.71 (0.67, 0.75)		0.70 (0.65, 0.74)*	
Not employed	0.61 (0.49, 0.71)		0.76 (0.68, 0.82)		0.39 (0.24, 0.52)*	
Age group		0.91[7]; 0.50[8]; 0.82[9]; 0.35[10]; 0.89[11]; 0.25[12]		0.58[7]; **0.05**[8]; **0.01**[9]; 0.11[10]; **0.002**[11]; 0.13[12]		0.46[7]; 0.10[8]; 0.37[9]; 0.30[10]; 0.90[11]; 0.33[12]
30-39 years	0.68 (0.55, 0.77)		0.61 (0.47, 0.72)*		0.75 (0.65, 0.82)	
40-49 years	0.68 (0.59, 0.76)		0.65 (0.55, 0.73)*		0.71 (0.62, 0.77)	

50-59 years	0.63 (0.54, 0.70)		0.73 (0.67, 0.79)*		0.65 (0.57, 0.72)	
60+ years	0.69 (0.62, 0.75)		0.79 (0.74, 0.84)*		0.70 (0.63, 0.76)	
PA guidelines[b]		0.19		0.77		0.12
Meets	0.71 (0.64, 0.76)		0.75 (0.69, 0.79)		0.73 (0.67, 0.78)	
Does not meet	0.67 (0.60, 0.70)		0.73 (0.69, 0.77)		0.69 (0.64, 0.74)	

[a] Pre-/Post-survey Spearman correlations and 95% confidence intervals

[b] U.S. Federal Physical Activity Guideline adherence defined using accelerometer MVPA bout data

* Indicate significant difference(s) between strata. ** *p* value for difference between Spearman ρ among strata calculated using Fisher's *z* test: [1]Latino, white; [2]black, white; [3]Latino, black; [4]normal weight, overweight; [5]normal weight, obese; [6]overweight, obese; [7]age 30-39, 40-49; [8]age 30-39, 50-59; [9]age 30-39, 60+; [10]age 40-49, 50-59; [11]age 40-49, 60+; [12]age 50-59, 60+.

Table 3.3 Correlations for total sedentary time estimated from post-test survey, seven-day diary, and accelerometry, Pearson *r*

	Survey vs. Diary r_{DS} (95% CI)[a]	*p* value** DS	Survey vs. Accelerometer r_{AS} (95% CI)	*p* value** AS	Accelerometer vs. Diary r_{AD} (95% CI)	*p* value** AD
All	0.53 (0.47, 0.58)		0.41 (0.35, 0.47)		0.56 (0.51, 0.61)	
Sex		0.10		0.34		0.17
Women	0.58 (0.51, 0.64)		0.39 (0.31, 0.47)		0.53 (0.41, 0.60)	
Men	0.49 (0.39, 0.57)		0.48 (0.38, 0.56)		0.58 (0.50, 0.65)	
Race/Ethnicity		0.27[1]; 0.20[2]; 0.95[3]		0.25[1]; 0.49[2]; 0.66[3]		0.19[1]; 0.81[2]; 0.36[3]
Black	0.46 (0.32, 0.59)		0.38 (0.23, 0.51)		0.57 (0.44, 0.67)	
White	0.56 (0.49, 0.62)		0.44 (0.36, 0.51)		0.58 (0.52, 0.64)	
Latino/a	0.47 (0.31, 0.60)		0.33 (0.16, 0.49)		0.48 (0.32, 0.61)	
BMI (kg/m^2)		0.85[4]; 0.46[5]; 0.75[6]		0.96[4]; 0.82[5]; 0.48[6]		0.90[4]; 0.11[5]; 0.13[6]
Normal weight	0.52 (0.42, 0.60)		0.41 (0.32, 0.50)		0.58 (0.50, 0.66)	
Overweight	0.50 (0.40, 0.59)		0.41 (0.29, 0.50)		0.58 (0.49, 0.65)	
Obese	0.56 (0.44, 0.65)		0.39 (0.25, 0.51)		0.48 (0.36, 0.59)	
Education		0.71		0.36		0.08
HS/some college	0.52 (0.41, 0.62)		0.38 (0.25, 0.50)		0.48 (0.36, 0.59)	
College grad	0.55 (0.48, 0.60)		0.44 (0.37, 0.51)		0.59 (0.53, 0.64)	
Employment		0.15		0.27		0.92
Employed	0.55 (0.49, 0.61)		0.43 (0.36, 0.50)		0.57 (0.51, 0.62)	
Not employed	0.45 (0.30, 0.57)		0.34 (0.18, 0.48)		0.57 (0.44, 0.68)	
Age group		**0.01**[7]; **0.02**[8]; **0.01**[9]; 0.68[10]; 0.76[11]; 0.44[12]		0.18[7]; 0.09[8]; 0.30[9]; 0.72[10]; 0.66[11]; 0.38[12]		0.53[7]; **0.01**[8]; 0.46[9]; **0.01**[10]; 0.92[11]; **0.01**[12]
30-39 years	0.72 (0.60, 0.80)*		0.53 (0.36, 0.57)		0.67 (0.54, 0.76)*	
40-49 years	0.51 (0.38, 0.61)*		0.39 (0.25, 0.51)		0.62 (0.51, 0.70)*	
50-59 years	0.54 (0.43, 0.62)*		0.36 (0.24, 0.47)		0.43 (0.32, 0.53)*	
60+ years	0.48 (0.38, 0.58)*		0.43 (0.32, 0.53)		0.61 (0.52, 0.69)*	
PA guidelines[b]		0.36		0.45		0.72

Meets	0.56 (0.47, 0.64)	0.45 (0.34, 0.54)	0.56 (0.47, 0.64)
Does not meet	0.51 (0.44, 0.58)	0.40 (0.32, 0.48)	0.58 (0.51, 0.64)

[a] Pearson bivariate correlation coefficients and 95% confidence intervals. Pearson correlation coefficients shown here were used to calculate VCs.

[b] U.S. Federal Physical Activity Guideline adherence defined using accelerometer MVPA bout data

* Indicate significant difference(s) between strata. ** *p* value for difference between Spearman ρ among strata calculated using Fisher's *z* test: [1]Latino, white; [2]black, white; [3]Latino, black; [4]normal weight, overweight; [5]normal weight, obese; [6]overweight, obese; [7]age 30-39, 40-49; [8]age 30-39, 50-59; [9]age 30-39, 60+; [10]age 40-49, 50-59; [11]age 40-49, 60+; [12]age 50-59, 60+.

Table 3.4 Validity estimates of total minutes sitting/day using method of triads, Validity Coefficients (VC)

	N	**VC_{ST}[a] (95% CI)**
All	713	0.62 (0.55, 0.69)
Sex		
Women	423	0.65 (0.54, 0.74)
Men	290	0.63 (0.51, 0.75)
Race/Ethnicity		
Black	136	0.56 (0.33, 0.75)
White	469	0.65 (0.56, 0.73)
Latino/a	108	0.57 (0.33, 0.80)
Body mass index (kg/m^2)		
Normal weight	282	0.60 (0.48, 0.72)
Overweight	249	0.59 (0.47, 0.70)
Obese	172	0.67 (0.48, 0.84)
Education		
HS or some college	182	0.64 (0.47, 0.79)
College grad and beyond	530	0.64 (0.56, 0.72)
Employment status		
Employed	574	0.65 (0.56, 0.72)
Not currently employed	132	0.51 (0.33, 0.68)
Age group		
30-39 years	97	0.75 (0.63, 0.88)*
40-49 years	167	0.56 (0.36, 0.75)
50-59 years	219	0.68 (0.53, 0.83)
60+ years	230	0.59 (0.46, 0.71)*
PA guidelines[b]		
Meets	279	0.69 (0.58, 0.73)*
Does not meet	434	0.58 (0.47, 0.67)*

[a] Validity coefficients (VC) between POST-survey and 'true' latent time spent sitting

[b] U.S. Federal Physical Activity Guideline adherence defined using accelerometer MVPA bout data

* Indicate significant difference(s) between strata.

Table 3.5 Sensitivity analysis among participants with seven valid days of accelerometer and diary data, validity estimates of total minutes sitting/day using method of triads, Validity Coefficients (VC)

	N (% of original sample)	VC_{ST}[a] (95% CI)
All	566 (79.4%)	0.65 (0.58, 0.72)
Sex		
Women	330 (78.0%)	0.68 (0.58, 0.77)
Men	236 (81.4%)	0.63 (0.50, 0.73)
Race/Ethnicity		
Black	91 (66.9%)	0.61 (0.34, 0.84)
White	390 (83.2%)	0.65 (0.56, 0.74)
Latino/a	85 (78.7%)	0.62 (0.37, 0.80)
Body mass index (kg/m^2)		
Normal weight	241 (85.5%)	0.62 (0.52, 0.72)
Overweight	201 (80.7%)	0.58 (0.42, 0.71)
Obese	115 (66.9%)	0.56 (0.34, 0.77)
Education		
HS or some college	138 (75.8%)	0.62 (0.44, 0.78)
College grad and beyond	427 (80.6%)	0.67 (0.58, 0.75)
Employment status		
Employed	451 (78.6%)	0.67 (0.59, 0.74)
Not currently employed	110 (83.3%)	0.54 (0.32, 0.73)
Age group		
30-39 years	78 (80.1%)	0.75 (0.59, 0.89)
40-49 years	120 (71.9%)	0.66 (0.47, 0.83)
50-59 years	177 (80.8%)	0.64 (0.48, 0.80)
60+ years	191 (83.4%)	0.61 (0.48, 0.73)
PA guidelines[b]		
Meets	231 (82.8%)	0.69 (0.57, 0.80)
Does not meet	335 (77.2%)	0.61 (0.50, 0.71)

[a] Validity coefficients (VC) for POST-survey + ’true’ latent value

[b] U.S. Federal Physical Activity Guideline adherence defined using accelerometer MVPA bout data

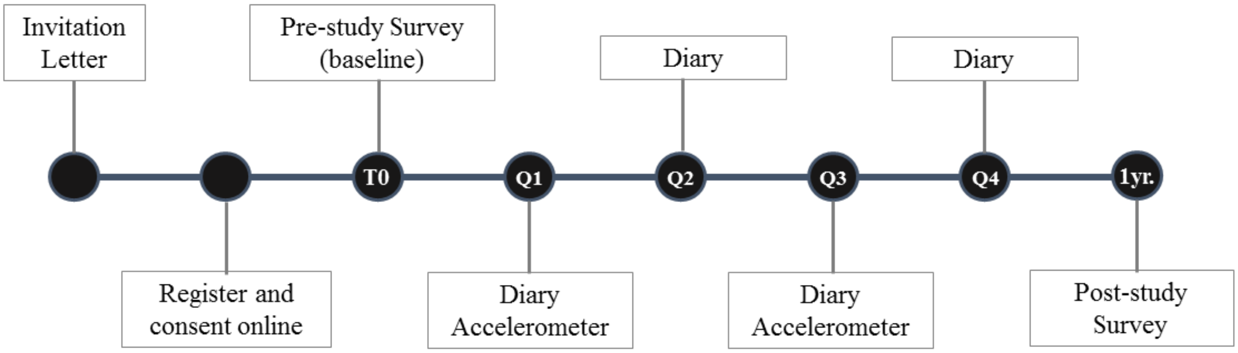

Figure 3.1 Example timeline of the CPS-3 AVSS. Note that half of the AVSS participants received the accelerometers during Q1 and Q3, while the other half received accelerometers during Q2 and Q4.

CHAPTER 4

RELIABILITY AND VALIDITY OF THE CANCER PREVENTION STUDY-3 PHYSICAL ACTIVITY SURVEY[2]

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[2] Rees-Punia E, Matthews CE, Evans EM, Keadle SK, Anderson RL, Gay JL, Schmidt MD, Gapstur SM, Patel AV. To be submitted to *American Journal of Epidemiology*.

4.1. Abstract

PURPOSE: This study examined the one-year test-re-test reliability and criterion validity of light (LPA), moderate (MPA), vigorous (VPA), and moderate-to-vigorous (MVPA) intensity physical activity survey items in a subset of participants from a large, nationwide prospective cohort.

METHODS: Participants included 423 women and 290 men aged 31-72 years in the Cancer Prevention Study-3 (CPS-3). Reliability was assessed by computing Spearman correlation coefficients between responses from pre- and post-study surveys for two separate CPS-3 PA grids. Validity was assessed by comparing PA estimated from the two CPS-3 grids with PA estimated from accelerometry and seven-day diaries. CPS-3 survey-estimated intensity-specific PA was also compared with a latent variable representing true PA estimated from the seven-day diaries, accelerometry, and surveys through the method of triads.

RESULTS: Reliability was generally considered acceptable or strong for all items on the detailed PA grid (range: ρ = 0.45-0.92) and acceptable for items on the abbreviated PA grid (range ρ = 0.37-0.61). Validity coefficients (VCs) for LPA were higher for the abbreviated PA grid, while VCs for MPA, VPA, and MVPA were higher for the detailed PA grid. On average, estimates of MVPA were 21.8 min/day higher on the abbreviated PA grid (95% limits of agreement: -140.6 min/day to 184.3 min/day) and 17.3 min/day higher on the detailed PA grid (95% limits of agreement: -96.8 to 62.2 min/day) compared to accelerometry.

CONCLUSION: The two CPS-3 PA grids have acceptable reliability and validity for ranking or categorizing participants according to overall PA or intensity-specific activity level.

4.2. Introduction

Physical inactivity has been associated with a higher risk of various adverse health outcomes including cardiovascular disease, certain types of cancer, and early mortality.(1-3) Much of what has been discovered about the relationship between physical activity (PA) and health is based on data collected by various self-reported measures. Although self-reported measures of PA may be influenced by participant comprehension, difficulty recalling events, social desirability bias and/or other sources of random and systematic error, surveys remain the most feasible and cost-effective option for large-scale epidemiologic studies.(4-6) Given this potential for bias within PA survey data, it is of upmost importance to conduct reliability and validity studies of new PA surveys.

PA is a multifaceted behavior which can be quantified by frequency, intensity, and duration. Because of the likelihood for the volume and intensity of PA to be differentially associated with various aspects of health, it is important to accurately measure each facet. Studies often report associations of PA volume with health, but there is new interest in the role of specific PA intensities. The intensity of an activity is classified by metabolic equivalents (METs), or the ratio of energy required for a specific activity compared to the energy required at rest. Light physical activities (LPAs) are activities requiring less than 3.0 METs, while moderate and vigorous activities (MPAs, VPAs) require between 3.0-6.0 and over 6.0 METs, respectively.(7, 8) There has been new interest, for example, in the role of LPA in weight loss and chronic disease prevention, as LPA may be viewed as more attainable by less fit individuals and is a major contributor to total physical activity energy expenditure.(9, 10) Although most prior validation studies generally focus on total PA or MVPA, it is important to demonstrate good validity in the ability to measure intensity-specific PA given the increasing interest in their associations with health.

The Cancer Prevention Study-3 (CPS-3) is an on-going prospective study of cancer incidence and mortality initiated by the American Cancer Society (ACS).(11) The CPS-3 survey assesses physical activity through one of two recall questions depending on the survey year: an abbreviated PA grid or a longer, more detailed PA grid. As it is expected that CPS-3 data will provide relevant information about PAand chronic disease in the future, it is important to understand the reliability and validity of the CPS-3 physical activity questionnaire. Furthermore, as newer epidemiologic cohorts collect PA data, utilization of a similar survey instrument would not only allow for high-quality data collection, but also allow for future harmonization of data across studies.

The present study sought to examine the one-year test-retest reliability and criterion validity of the LPA, MPA, VPA, and MVPA items from the CPS-3 questionnaire in a subset of participants from a large, nationwide prospective cohort study of U.S. adults. Secondarily, this study aimed to evaluate the reliability and validity estimates of the PA survey items stratified by sex and race/ethnicity. Results from this study will enable understanding of CPS-3 findings related to PA, guide future use of this questionnaire, and help inform survey design and/or survey selection decisions for future epidemiologic studies of PA.

4.3. Methods

Study Population

CPS-3 participants were recruited at ACS fundraising events or community enrollment drives between 2006 and 2013.(11) Over 304,000 participants aged 30 to 65 years with no history of cancer (except for basal or squamous cell skin cancer) were enrolled. CPS-3 participants completed a baseline survey at enrollment, and are sent repeat surveys every three years to update exposure information.

In 2015, CPS-3 participants were stratified by sex and race/ethnicity and randomly invited to participate in the CPS-3 Activity Validation Sub-study (CPS-3 AVSS). Among the 10,000 participants invited, 1,801 participants pre-registered and consented to participate in the AVSS, and the first 300 white women, 150 white men, 150 Latino/as, and 150 African American/Black participants to complete the 2015 CPS-3 follow-up survey were enrolled into the AVSS. In total, 751 participants were enrolled in the CPS-3 AVSS. All aspects of the CPS-3 are approved by the Institutional Review Board at Emory University.

AVSS Participants were sequentially excluded from the current analyses for the following reasons: having four quarters of invalid diary data (n = 1), lacking sufficient accelerometer wear (≥4 days, ≥10 hours/day wear time) within the range of valid diary dates (n = 25), or missing pre- or post-survey physical activity information (n = 12).

Study Design

At the start of the CPS-3 AVSS, participants received a four-page ‘pre-study survey’ which included both PA questions and various demographic items. Subsequent data collection occurred over the following year, which was split into four equal quarters. During each of the four quarters, participants completed a seven-day diary, and during two non-consecutive quarters, participants wore accelerometers concurrent with diaries. Approximately one year after completing the pre-study survey, participants completed the same four-page survey once again (the ‘post-study survey’). Participants could receive a maximum incentive of $100 upon completion of the AVSS, with deductions for incomplete diaries ($20) or lost accelerometers ($25).

Measures

Seven-Day Diary: Participants completed one seven-day diary for each quarter of the study, during which they were asked to code their activities in 15-minute epochs throughout the entire day on seven consecutive days. Codes aligning with LPA included: “standing, very light activities, showering, dressing, etc.” and “walking (at a pace less than 3 mph), light activity, stretching, yoga, childcare, cooking, light yard work, household chores, light weightlifting, calisthenics”. Diary codes aligning with MVPA included: “walking (at pace of 3 to 3.9 mph), dancing, cycling (less than 10 mph), gardening, heavy yard word, mowing lawn, golfing without a cart” (moderate), “walking (at least 4 mph), recreational basketball, softball, baseball, hiking” (moderate), “cycling (10 to 13.9 mph), swimming, recreational sports (tennis, racquetball, soccer), aerobics, skiing, heavy weightlifting” (vigorous), “jogging (less than 6 mph), elliptical or stair climbing, competitive sports (basketball, flag football), boxing” (vigorous), and “vigorous lap swimming, running (at least 6 mph), cycling (14+ mph), intense manual work” (vigorous). Days with fewer than 10 waking hours reported were considered invalid and excluded from the analysis. Daily average minutes of LPA, MPA, VPA, and MVPA were calculated as a weighted average for quarters with a minimum of four valid days. Quarterly values were further averaged to generate mean daily minutes of PA which account for seasonal changes in behavior.

Accelerometer: During two non-consecutive quarters (Q1/Q3 or Q2/Q4), participants wore an Actigraph GT3x accelerometer on the hip aligning with the midline of the non-dominant thigh. Participants were instructed to wear the device for seven consecutive days concurrent with the seven-day diary during all waking hours, except when bathing or participating in water-based activities. Accelerometer data recorded on invalid diary dates were excluded to maintain an overlap in valid accelerometer/diary days.

Raw Actigraph data were processed using the Choi algorithm to calculate accelerometer wear time and the sojourn-3 axis algorithm to estimate daily sedentary time.(12-15) The sojourn-3 axis method is a hybrid machine-learning, neural network, and decision tree analysis algorithm which uses second-by-second triaxial accelerometer counts to estimate free-living PA.(14) Days failing to meet the wear time minimum of 10 hours/day were excluded from the analysis. Daily average minutes of LPA, MPA, VPA, and MVPA were calculated as a weighted average for quarters with a minimum of four valid days.(16) Quarterly values were further averaged to generate mean daily minutes of PA which account for seasonal changes in behavior.

Survey: Participants completed the same four-page survey at the beginning and end of the one-year validation study. Information on PA was collected using two PA grids. The abbreviated PA grid captured the typical 24-hour period on a weekday or weekend day by asking, “During **the past year**, estimate the **hours per day** you spent on **typical weekdays and weekends** in each of the following activities. Please average your seasonal physical activities over the entire year. **Try to account for all 24 hours per day**” included the brief responses: “standing or moving about” and “light activities” for LPA, as well as “weight lifting or resistance exercise” and “moderate activities” for MPA, and “strenuous activities” for VPA. An item for walking was also included on this question, but as pace could not be determined, walking was not included in the MVPA calculation. Responses to each activity item included “0, <1, 1-2, 3-4, 5-6, 7-8, 9-10, 11+” hours per day for the typical weekday and weekend day separately. The mean number of hours within the response categories (0, 0.5, 1.5, 3.5, 5.5, 7.5, 9.5, and 11 hours per day) were summed for each PA intensity level, and weighted averages for daily minutes of LPA, MPA, VPA, and MVPA were calculated.

The CPS-3 survey also included a more detailed PA grid focused primarily on leisure-time activities: “During the **past year**, estimate how many **hours per week** and **months per year** you spent in each of the following activities: calisthenics (Pilates, sit-ups, pushups, etc.), yoga or Tai Chi, yard work or home maintenance (leisure-time LPAs); lap swimming, aerobics class, elliptical or other aerobic machine, dancing, other aerobic recreation (golf without a cart, hiking, skiing, etc.), and weight training or resistance exercises (MPAs); jogging, running, tennis or racquetball, sports activities (VPAs); walking”. The question “What is your usual walking pace outdoors” was used to determine the intensity of walking for the detailed PA questionnaire. Walking by participants selecting “easy, causal (less than 2mph)” was classified as LPA, while walking by participants selecting “normal, average (2-2.9mph)”, “brisk pace (3-3.9mph)”, or “very brisk/striding (4mph or faster)” was classified as MVPA. Responses to each individual activity included: “none, <1, 1-2, 3, 4-6, 7+” hours per week and “1-3, 4-6, 7-9, 10-12” months per year. The mean number of hours within the response categories (0, 0.5, 1.5, 3, 5, and 7 hours per day) were summed for each PA intensity level, and multiplied by the proportion of the year active (0.25, 0.5, 0.75, 1) to generate average daily minutes spent at each PA intensity.

Statistical Analysis

Reliability of specific survey items was assessed by calculating Spearman correlation coefficients (ρ) between the pre- and post-survey responses for each individual item of each questionnaire. Reliability estimates were also calculated stratified by sex and race/ethnicity. Differences among subgroups were tested for statistical significance using Fisher's *z* test.

Pearson correlation coefficients (r) and Bland-Altman plots with 95% limits of agreement were calculated for both PA surveys.(17) Survey validity was also assessed via the method of triads. Based on factor analysis theory, the method of triads can be used to estimate model parameters which define the theoretical relationship between three measured exposures and the 'true' latent (unobserved) exposure.(18, 19) This method is particularly useful as measurement error associated with accelerometers, diaries, and recall surveys may be correlated. This can be problematic as traditional validation approaches (for example, correlations between two measures) technically require independent measurement error between the two measures.(18) Further, it has been suggested that the combination of methods may result in an improved estimation of true exposure.(20) Although the method of triads is not yet commonly used in PA survey validation studies, it has been used extensively in nutritional epidemiology and psychology validation studies and can realistically be applied in the validation of any continuous exposure measure.

The method of triads encompasses calculating three validity coefficients (VC), which are correlations between the 'true' time spent physically active at each respective intensity and the measured time spent physically active. VCs are calculated using a set of three pairwise correlation coefficients (Pearson r) among the accelerometer, the seven-day diary, and the post-study survey in the following formulas:

$$VC_{AT} = \sqrt{r_{AD} * r_{AS} / r_{DS}}$$

$$VC_{DT} = \sqrt{r_{AD} * r_{DS} / r_{AS}}$$

$$VC_{ST} = \sqrt{r_{AS} * r_{DS} / r_{AD}}$$

Where A, D, and S are the measurements from the accelerometer, diary, and survey, respectively, and VC_{AT}, VC_{DT}, and VC_{ST} are the validity coefficients between the 'true' time spent physically active at a light, moderate, or vigorous intensity and the accelerometer-measured, diary estimated, and post-study survey estimated active time, respectively. Bootstrapping methods were used to calculate 95% confidence intervals.(21) The method of triads was also used to calculate criterion validity estimates and bootstrap 95% confidence intervals stratified by sex and race/ethnicity. A sensitivity analysis was conducted restricting to participants with seven valid days of diary data and seven valid days of accelerometer data defined using a 14-hour wear time minimum (n=566). As the CPS-3 AVSS participants were much more active than the general U.S. population, an additional sensitivity analysis excluding participants falling above the 95th percentile of MVPA min/day from the 2015 National Health Interview Survey was conducted (n=480).(22)

4.4. Results

Overall, 423 women and 290 men with a mean age of 51.7 (range 31-72) years were included in these analyses. Baseline characteristics are shown in Table 4.1. Overall, participants recorded diary data for an average of 6.7 days per quarter and 16.8 (± 2.8) waking hours per day, and wore the accelerometers for an average of 6.6 days per quarter for 16.1 (± 1.6) hours per day. Participants reported an average of 56 (± 40) min/d of MVPA on the detailed PA grid. Compared to the accelerometer and diary, participants reported more MVPA on the abbreviated PA grid (93 ± 78 min/d). Similarly, participants reported an average of 357 (± 169) min/d LPA on the abbreviated grid, compared to 270 (± 84) min/d and 343 (± 125) min/d via accelerometry and diary, respectively. Reflecting the intended purpose of the detailed survey to measure MVPA, participants only reported an average of 27 (± 21) min/d LPA on the detailed grid.

One-year repeatability estimates of the CPS-3 PA items are shown in Table 4.2. For the abbreviated PA grid, the highest Spearman correlation coefficient was seen for the strenuous activities item (0.61), followed by the weight lifting item (0.59). The walking (0.39) and light activities (0.37) items had the lowest reliability estimates. There were no significant differences in reliability by sex or race/ethnicity for the abbreviated PA grid items (race/ethnicity data not shown). Overall, reliability was generally considered acceptable or strong for the detailed PA grid. The tennis item had the highest reliability (0.92), while elliptical/rowing machines had the worst (0.45). There were several differences in reliability estimates by sex for the detailed PA items. Reliability estimates were significantly higher among men for the running, bicycling, tennis, yoga, weight training, and yard work items, but significantly higher among women for the jogging, aerobics class, and sports items ($p<0.05$).

Pearson correlation coefficients for each pair of the four PA measures were calculated and used to create VCs (Table 4.3). Briefly, LPA measured by the abbreviated PA grid was more highly correlated with accelerometer and diary measured LPA, while MPA, VPA, and MVPA measured by the detailed grid was more highly correlated with accelerometer and diary measures. Figure 4.1 illustrates the agreement of MVPA measured by each CPS-3 PA question with accelerometry for individual participants. On average, estimates of MVPA were 21.8 min/d higher on the abbreviated PA grid compared to accelerometry (95% limits of agreement ranging from -140.6 min/d to 184.3 min/d), and 17.3 min/d higher with the detailed grid compared to accelerometry (95% limits of agreement ranging from -96.8 to 62.2 min/d).

Among all participants, VCs for LPA were higher for the abbreviated PA grid, while VCs for MPA, VPA, and MVPA were higher for the detailed PA grid (Table 4.4). VCs for both questions and all PA intensities indicated fair or acceptable agreement. There were no significant differences in VCs by sex or race/ethnicity for the abbreviated PA grid items. VCs for VPA measured via the detailed PA grid were significantly different by sex only ($p<0.01$). Very similar results were seen when restricting to participants with seven days of data and participants reflecting the MVPA patterns of the U.S. population (Table 4.5). Given the limited ability to classify walking intensity due to missing pace information on the abbreviated survey, results were stratified by reported walking time (Table 4.6). VCs for participants reporting the least amount of walking were significantly higher than participants reporting more walking for LPA, MPA, and MVPA.

4.5. Discussion

Even in large epidemiologic studies where some amount of random error or bias is expected and manageable, it is important to ensure a certain level of validity in exposure measures such as PA questionnaires. Given the relatively new research interest in specific intensities of PA, it is imperative to assure that PA questionnaires are valid for the specific purpose of measuring time spent in each PA intensity.(5, 23) In the current study, the CPS-3 PA questionnaires were found to be reliable and valid in terms of ranking or classifying participants according to PA frequency, duration, intensity, and to some extent, PA type.

Overall, the results of the current study comport well with studies of PA questionnaires with similar survey characteristics. Reliability estimates (Spearman ρ) for the CPS-3 questionnaires ranged from 0.37-0.61 for the abbreviated PA grid and 0.45-0.92 for the detailed

PA grid. With a few exceptions, these values fall within the median reliability estimates of 0.62-0.76 reported in a large systematic review of over 100 PA questionnaires.(24) This review also found that higher reliability coefficients were more likely when study protocols included shorter test-retest periods, which is an important finding given the very long test-retest period in the CPS-3 AVSS. It is important to note that the average number of min/d spent in MVPA estimated using the abbreviated PA grid was considerably higher than the amount estimated using the seven-day diary or accelerometer. However, the mean daily minutes of MVPA estimated using the detailed PA grid fell between the mean amount of MVPA estimated from the diary and accelerometer. These data are generally consistent with prior reviews which suggest that PA questionnaires tend to overestimate MVPA.(24) Validity estimates for MVPA measured via CPS-3 PA questions compared to accelerometer-measured MVPA were similar to those reported in other studies. For example, one study reported Pearson correlations between 0.39 and 0.44 for total PA measured through survey and accelerometer, which are very similar to validity estimates of the CPS-3 abbreviated grid (r = 0.41) and detailed grid (r = 0.35) for MVPA. (25) Among the very few studies that reported validity estimates specifically for VPA, a review of the International PA Questionnaire-Short Form (IPAQ-short) reported correlations with accelerometer-measured VPA ranging from -0.03-0.47 (Spearman ρ).(26) Another study exploring VPA-specific validity reported correlations of similar magnitude, but found a significant difference in the validity of survey-measured VPA by sex (ρ = 0.39 for women and ρ = 0.31 for men, $p_{int.}$ = 0.034). (20) Although there were no significant differences by sex for the validity of VPA measured by either CPS-3 question and accelerometry, the correlations were similar to these prior studies (r = 0.32 for abbreviated grid and 0.47 for detailed grid). Additionally, the mean differences in MVPA generated from the Bland-Altman plots in the current study (17.3 min/day for the detailed grid and 21.8 min/day for the abbreviated grid) are only marginally higher than the mean difference between the European Health Interview Survey (EHIS) and accelerometer estimated MVPA (-11.7 min/day). (27) Finally, further evidence of the acceptable validity of the CPS-3 survey is demonstrated by the overall VCs for each PA intensity measured by both questions. Together, these results suggest that the CPS-3 questions are suitable for ranking or classifying participants according to PA dose (including duration and intensity), but may not be suitable for detecting small changes in PA time.

The PA intensity-specific results from the current study merit additional comment, especially as prior research in this area is limited. LPA, a large contributor to total PA energy expenditure, can be difficult to measure accurately via survey.(10) As the majority of our waking active time is spent on LPA, it can be difficult for participants to recall time spent on common, unremarkable activities such as standing and walking about or home maintenance. Regardless, reliability for these items was acceptable in the CPS-3 questionnaire ($\rho = 0.51$ for standing from the abbreviated grid and $\rho = 0.57$ for yard work or home maintenance from the detailed grid). Despite acceptable reliability, the list of LPA items was not extensive enough to fully capture LPA. As a result, correlations with accelerometer-measured LPA were poor ($r = 0.29$ abbreviated grid with accelerometer, $r = 0.16$ detailed grid with accelerometer). MPA, VPA, and MVPA estimated with the detailed grid had higher validity than the abbreviated grid. This is likely due to the major limitation of the abbreviated grid: the lack of information on walking pace/intensity. Because reported walking could not be classified as MVPA on the abbreviated grid, it was not included in the MVPA totals. However, the role of this limitation in the lower than expected validity of MPA and MVPA could be confirmed by stratifying by reported walking time. VCs for participants reporting the least amount of walking were significantly higher than participants reporting more walking for LPA, MPA, and MVPA, suggesting that the misclassification of walking intensity influenced the observed validity estimates of the abbreviated grid. Based on what was learned in the current study, future CPS-3 abbreviated PA grids will include two walking items: “walking less than 3 mph or slower than 20 minutes per mile” and “walking 3+ mph or faster than 20 minutes per mile”.

This study had several strengths. The large, diverse sample allowed for the examination of measure bias in certain sub-groups. Additionally, validity evidence from a variety of measures was possible through the use of accelerometers and diaries- both of which had very high participant compliance (i.e., high accelerometer wear time averages and complete diary data). This study also provides validity estimates for each PA intensity. Intensity-specific data were largely missing from prior validation studies which focused exclusively on total PA or MVPA, and are important as there is current interest in intensity-specific PAs such as LPA.

This study is not without limitations. It is possible that the very active and highly complaint CPS-3 AVSS participants are not representative of the underlying CPS-3 population. Participants may have also been motivated by the monetary incentive, although it is important to note that 18% of participants donated their study incentive back to the ACS. Another potential limitation of this study is the very long test-retest period. As the CPS-3 survey asks participants to report their PA during the past year, it is not possible to determine if changes in one-year responses are due to true changes in PA or poor reliability. Further, as with any study reliant on accelerometer data, the lack of agreement regarding cut-points for PA intensities and the various other processing decisions may influence results.(28) However, efforts were made to select algorithms which have been shown to provide optimal data when used in combination with a self-reported wear log.(29) Accelerometers also have a limited ability to measure non-ambulatory activities, which is pertinent as nearly 50% of the CPS-3 AVSS cohort reported biking and 15% reported swimming. It is important to consider that surveys capture perceived or relative intensity of PA, while accelerometers capture absolute intensity, when interpreting results. Finally, the limited ability to determine the PA intensity of walking on the abbreviated grid likely impacted validity estimates for MPA and MVPA.

Conclusions

The results of this study showed that the CPS-3 PA questions have acceptable reliability and validity, with estimates similar to those from other PA questionnaires or cohort surveys. The CPS-3 PA questions are suitable for ranking or categorizing participants according to overall PA level or intensity-specific activity level. These findings also suggest that participant responses are not systematically biased by sex or race/ethnicity, a finding many prior validation studies may have been too underpowered to detect.

4.6. References

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Table 4.1 Baseline characteristics, CPS-3 PA Validation Study

	N (%) or mean ± SD	**Mean daily MVPA-survey (min)[1]**	**Mean daily MVPA-survey (min)[2]**	**Mean daily MVPA-diary (min)**	**Mean daily MVPA-accel. (min)[†]**
All	713	93 ± 78	56 ± 40	41 ± 36	73 ± 29
Demographics					
Sex					
Men	290 (40.7%)	110 ± 89	52 ± 36	51 ± 42	78 ± 31
Women	423 (59.3%)	82 ± 68	62 ± 45	34 ± 30	70 ± 28
Race					
Black	136 (19.1%)	104 ± 95	53 ± 42	36 ± 35	67 ± 29
Latino/a	108 (15.1%)	75 ± 71	51 ± 40	36 ± 36	69 ± 26
White	469 (65.8%)	94 ± 74	58 ± 39	44 ± 36	76 ± 30
Age					
30-39 yr.	97 (13.5%)	79 ± 56	60 ± 41	35 ± 25	68 ± 29
40-49 yr.	167 (23.5%)	94 ± 79	56 ± 44	37 ± 33	72 ± 25
50-59 yr.	219 (30.8%)	103 ± 84	57 ± 40	44 ± 36	77 ± 29
60+ yr.	230 (32.3%)	90 ± 80	53 ± 37	43 ± 38	72 ± 32
BMI					
Underweight	7 (1.0%)	34 ± 36	57 ± 36	31 ± 26	55 ± 34
Normal weight	282 (39.7%)	100 ± 77	63 ± 40	47 ± 33	79 ± 31
Overweight	249 (35.1%)	93 ± 76	58 ± 41	43 ± 36	74 ± 29
Obese	172 (24.1%)	70 ± 62	33 ± 30	29 ± 48	61 ± 24
Missing	3 (0.4%)	106 ± 94	110 ± 60	47 ± 42	84 ± 38
Education					
HS or come college	182 (25.5%)	96 ± 84	55 ± 40	39 ± 36	74 ± 32
College grad	530 (74.4%)	93 ± 76	56 ± 40	42 ± 36	73 ± 28
Missing	1 (0.1%)	94 ± 0	55 ± 0	34 ± 0	64 ± 0
PA Guidelines[‡]					
Adheres	279 (39.1%)	108 ± 78	72 ± 39	60 ± 37	94 ± 27
Does not adhere	434 (60.9%)	84 ± 72	48 ± 38	31 ± 29	60 ± 23
Avg. accel wear time (min)	963.3 ± 165.5	-	-	-	-

Avg. diary waking time (min)	1009.9 ± 115.1	-	-	-	-

‡2008 U.S. Physical Activity Guideline adherence defined using accelerometer MVPA *bout* data

†*Non-bouted* minutes of MVPA

[1] Based on abbreviated PA grid (post)

[2] Based on detailed PA grid (includes walking where pace >2mph; post)

Table 4.2 Reliability for pre- and post-survey items, Spearman ρ

Survey Item	All, ρ	Males, ρ	Females, ρ	*p* int.
Abbreviated PA Grid				
Standing	0.51	0.45	0.54	0.122
Walking	0.39	0.46	0.34	0.054
Weight lifting	0.59	0.62	0.58	0.408
Light activities	0.37	0.38	0.35	0.638
Moderate activities	0.47	0.43	0.47	0.505
Strenuous activities	0.61	0.65	0.58	0.129
Detailed PA Grid				
Walking	0.46	0.47	0.45	0.820
Usual walking pace	0.64	0.63	0.64	0.818
Jogging	0.51	0.43	0.56	0.020*
Running	0.76	0.78	0.70	0.016*
Bicycling	0.77	0.79	0.70	0.007*
Tennis, Racquetball	0.92	0.94	0.89	0.0003**
Lap swimming	0.69	0.73	0.66	0.067
Aerobics class	0.55	0.46	0.56	0.015*
Elliptical, rowing, etc.	0.45	0.45	0.47	0.734
Sports	0.61	0.55	0.69	0.002*
Dancing	0.46	0.45	0.54	0.107
Other aerobic	0.49	0.45	0.55	0.072
Calisthenics	0.61	0.58	0.64	0.197
Yoga, Tai Chi	0.69	0.75	0.66	0.016*
Weight training	0.63	0.68	0.56	0.0008*
Yard work, home maintenance	0.57	0.67	0.51	0.0009*

*Significant at $p<.05$, **Significant at $p<.0001$

Table 4.3 Correlations for all pairs of PA measures, Pearson *r*

	All (n = 713), *r*	**Men (n = 290), *r***	**Women (n = 493), *r***	***p* int.**
LPA				
Survey[1] and Survey[2]	0.21	0.26	0.18	0.259
Survey[1] and Diary	0.49	0.45	0.51	0.294
Survey[1] and Accelerometer	0.29	0.27	0.29	0.772
Survey[2] and Diary	0.26	0.31	0.24	0.308
Survey[2] and Accelerometer	0.16	0.23	0.13	0.165
Diary and Accelerometer	0.44	0.42	0.44	0.741
MPA				
Survey[1] and Survey[2]	0.31	0.37	0.24	0.054
Survey[1] and Diary	0.22	0.13	0.27	0.049*
Survey[1] and Accelerometer	0.17	0.14	0.19	0.490
Survey[2] and Diary	0.27	0.18	0.34	0.021*
Survey[2] and Accelerometer	0.26	0.28	0.23	0.472
Diary and Accelerometer	0.37	0.36	0.36	0.992
VPA				
Survey[1] and Survey[2]	0.49	0.57	0.35	0.0002**
Survey[1] and Diary	0.54	0.56	0.51	0.347
Survey[1] and Accelerometer	0.32	0.28	0.33	0.459
Survey[2] and Diary	0.56	0.56	0.54	0.700
Survey[2] and Accelerometer	0.47	0.47	0.44	0.610
Diary and Accelerometer	0.47	0.38	0.55	0.003*
MVPA				
Survey[1] and Survey[2]	0.47	0.52	0.40	0.040*
Survey[1] and Diary	0.41	0.35	0.44	0.145
Survey[1] and Accelerometer	0.23	0.16	0.26	0.159
Survey[2] and Diary	0.51	0.49	0.51	0.719
Survey[2] and Accelerometer	0.35	0.37	0.31	0.362
Diary and Accelerometer	0.48	0.46	0.49	0.603

[1] Based on abbreviated PA grid (post)

[2]Based on detailed PA grid (includes walking where pace >2mph; post)
*Significant at $p<.05$, **Significant at $p<.0001$

Table 4.4 Method of triads validity coefficients (VC)

	VC^1 (CI)	**VC^2 (CI)**
All		
LPA	0.57 (0.47, 0.66)	0.31 (0.19, 0.42)
MPA	0.33 (0.20, 0.45)	0.44 (0.34, 0.53)
VPA	0.61 (0.50, 0.72)	0.75 (0.65, 0.84)
MVPA	0.36 (0.25, 0.47)	0.61 (0.52, 0.69)
Sex		
Men		
LPA	0.53 (0.34, 0.70)	0.41 (0.21, 0.61)
MPA	0.28 (0.08, 0.49)	0.36 (0.19, 0.51)
VPA	0.64 (0.39, 0.86)	0.83 (0.66, 0.98) *
MVPA	0.32 (0.13, 0.50)	0.62 (0.48, 0.75)
Women		
LPA	0.59 (0.44, 0.72)	0.27 (0.12, 0.44)
MPA	0.32 (0.13, 0.50)	0.47 (0.33, 0.62)
VPA	0.55 (0.43, 0.68)	0.64 (0.51, 0.76) *
MVPA	0.35 (0.18, 0.50)	0.58 (0.45, 0.70)

[1] Based on abbreviated PA grid (post)

[2] Based on detailed PA grid (includes walking where pace >2mph; post)

*Significant difference by sex, $p_{int} < 0.05$

Table 4.5 Sensitivity analyses: method of triads validity coefficients (VC)

	N (% of original sample)	**VC^1 (CI)**	**VC^2 (CI)**
Among participants with 7 d. data w/ 14 hr wear time min			
All	566 (79.3%)		
LPA		0.58 (0.47, 0.69)	0.34 (0.20, 0.47)
MPA		0.26 (0.09, 0.42)	0.41 (0.31, 0.53)
VPA		0.59 (0.46, 0.73)	0.71 (0.60, 0.81)
MVPA		0.31 (0.18, 0.44)	0.58 (0.48, 0.67)
Sex			
Men	236 (81.4%)		
LPA		0.56 (0.37, 0.73)	0.37 (0.14, 0.58)
MPA		0.27 (0.07, 0.52)	0.36 (0.15, 0.53)
VPA		0.59 (0.34, 0.83)	0.78 (0.61, 0.95)
MVPA		0.29 (0.09, 0.49)	0.62 (0.48, 0.75)
Women	330 (78.0%)		
LPA		0.59 (0.43, 0.73)	0.32 (0.15, 0.49)
MPA		0.20 (0.06, 0.36)	0.44 (0.29, 0.58)
VPA		0.59 (0.46, 0.71)	0.63 (0.46, 0.76)
MVPA		0.28 (0.13, 0.44)	0.53 (0.49, 0.66)
Among participants with MVPA reflective of U.S. population‡			
All	480 (67.3%)		
LPA		0.64 (0.53, 0.74)	0.30 (0.15, 0.44)
MPA		0.24 (0.08, 0.43)	0.41 (0.27, 0.55)
VPA		0.55 (0.43, 0.67)	0.61 (0.47, 0.76)
MVPA		0.24 (0.09, 0.42)	0.52 (0.39, 0.64)
Sex			
Men	174 (60.0%)		
LPA		0.57 (0.36, 0.75)	0.44 (0.22, 0.62)
MPA		0.29 (0.06, 0.59)	0.33 (0.13, 0.54)
VPA		0.59 (0.36, 0.82)	0.64 (0.40, 0.87)
MVPA		0.31 (0.09, 0.58)	0.49 (0.30, 0.71)
Women	306 (72.3%)		
LPA		0.64 (0.48, 0.78)	0.24 (0.07, 0.41)
MPA		0.25 (0.07, 0.46)	0.52 (0.25, 0.77)
VPA		0.57 (0.42, 0.71)	0.59 (0.41, 0.76)
MVPA		0.24 (0.06, 0.43)	0.56 (0.36, 0.74)

[1] Based on abbreviated PA grid (post-survey)

[2] Based on detailed PA grid (includes walking as moderate intensity where pace >2mph, else walking is light intensity; post-survey)

*Significant difference by sex, p_{int} <0.05

‡Both survey responses falling within 99th percentile of NHIS MVPA min/week

Table 4.6 Validity of abbreviated grid by reported walking time, method of triads validity coefficients (VC)

	Low walking **VC^1 (CI)**	**Moderate walking** **VC^1 (CI)**	**High walking** **VC^1 (CI)**
All	(N = 199)	(N = 265)	(N = 249)
LPA	0.82 (0.68, 0.98)	0.54 (0.38, 0.69)	0.38 (0.19, 0.56)
MPA	0.42 (0.17, 0.70)	0.26 (0.09, 0.43)	0.32 (0.10, 0.54)
VPA	0.65 (0.48, 0.80)	0.75 (0.58, 0.90)	0.54 (0.32, 0.75)
MVPA	0.56 (0.37, 0.74)	0.51 (0.35, 0.66)	0.31 (0.11, 0.50)
Sex			
Men	(N = 68)	(N = 115)	(N = 107)
LPA	0.62 (0.31, 0.88)*	0.60 (0.22, 0.96)	0.37 (0.09, 0.66)
MPA	0.51 (0.14, 1.00)	0.23 (0.04, 0.47)	0.26 (0.05, 0.51)
VPA	0.68 (0.38, 0.96)	0.76 (0.45, 1.00)	0.66 (0.28, 1.00)
MVPA	0.62 (0.29, 0.96)	0.39 (0.14, 0.61)	0.26 (0.06, 0.51)
Women	(N = 131)	(N = 150)	(N = 142)
LPA	0.90 (0.77, 1.00)*	0.47 (0.23, 0.71)	0.40 (0.16, 0.61)
MPA	0.41 (0.16, 0.67)	0.41 (0.16, 0.67)	0.42 (0.10, 0.82)
VPA	0.65 (0.41, 0.84)	0.72 (0.53, 0.90)	0.46 (0.25, 0.66)
MVPA	0.53 (0.31, 0.71)	0.58 (0.38, 0.75)	0.38 (0.12, 0.66)

[1] Based on abbreviated PA grid (post); walking tertiles

*Significant difference by sex, $p_{int} < 0.05$

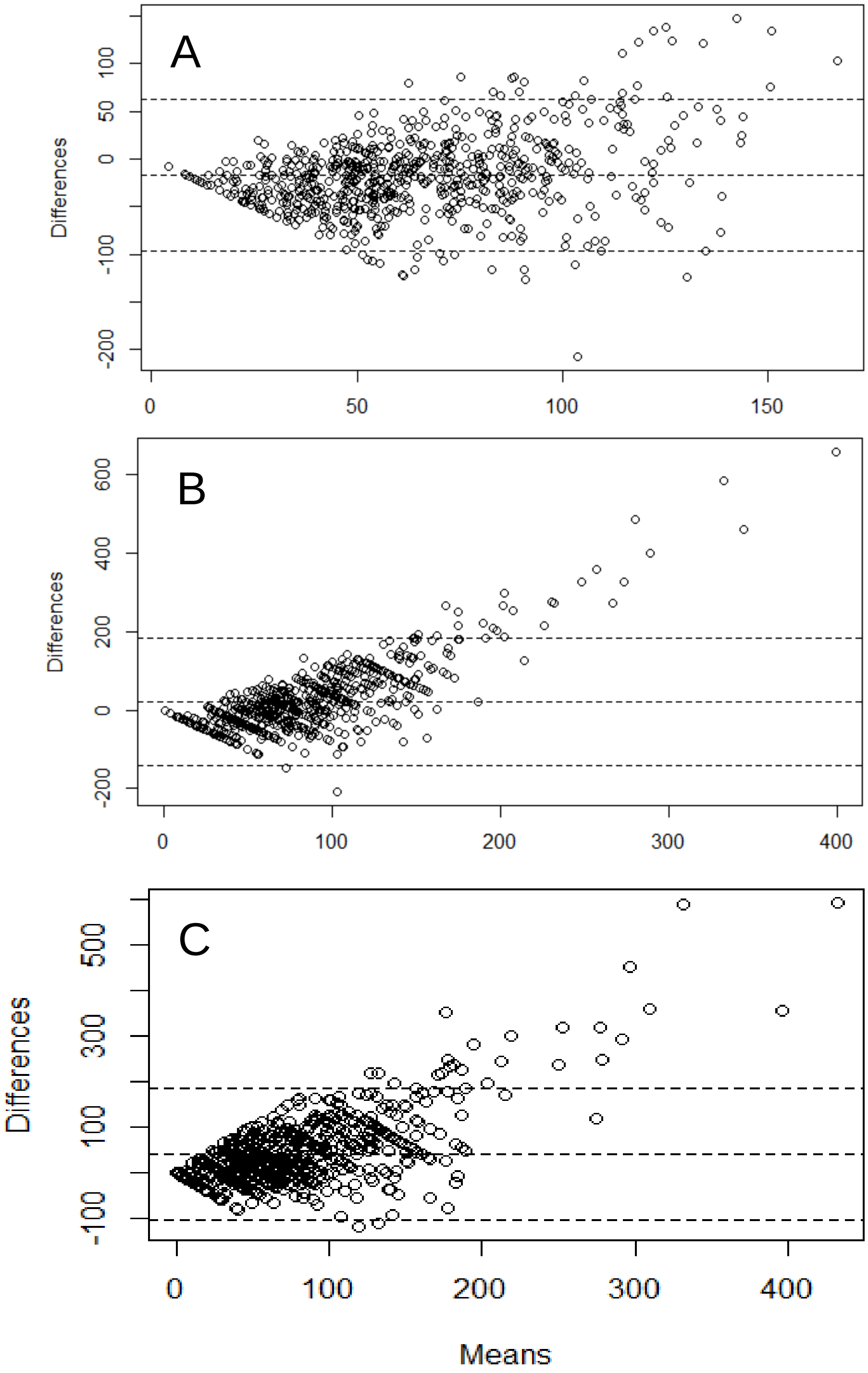

Figure 4.1. Bland-Altman plots of MVPA min/d. A. abbreviated and detailed CPS-3 surveys, mean difference = 39.13, 95% limits of agreement= -106.60 to 184.86. B. abbreviated CPS-3 survey and accelerometer, mean difference = 21.83, 95% limits of agreement= -140.62 to 184.28. C. detailed CPS-3 survey and accelerometer, mean difference = 17.30, 95% limits of agreement= -96.78 to 62.17.

CHAPTER 5

MORTALITY RISK REDUCTIONS FOR REPLACING SEDENTARY TIME WITH PHYSICAL ACTIVITIES[3]

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[3] Rees-Punia E, Schmidt MD, Evans EM, Gay JL, Matthews CE, Gapstur SM, Patel AV. To be submitted to the *American Journal of Preventative Medicine*.

5.1. Abstract

Introduction: Insufficient physical activity is a well-established risk factor for early mortality. Recent evidence suggests that excess sitting may be an additional risk factor, independent of insufficient physical activity. This may be due, at least in part, to the displacement of physical activities with sedentary behaviors. The purpose of this study was to examine the mortality risk reductions associated with replacing 30 min·day^{-1} sitting for an equivalent duration of light or moderate-to-vigorous intensity physical activity (LPA, MVPA).

Methods: Participants included 40,866 men and 60,891 women in the Cancer Prevention Study-II Nutrition Cohort. An isotemporal substitution approach to Cox proportional hazards regression models was used to estimate adjusted hazard ratios (HR) and 95% confidence intervals (HR, 95% CI) for mortality associated with the substitution of 30 min·day^{-1} sitting for LPA or MVPA.

Results: During 13 years of follow-up, 16,163 men and 15,638 women died. Among the least active participants, the replacement of 30 min·day^{-1} sitting with LPA was associated with a 14% mortality risk reduction (HR=0.86, 0.83-0.89) and replacement with MVPA was associated with a 50% mortality risk reduction (HR=0.50, 0.44-0.58). Similar associations were seen among moderately active participants (HR=0.91, 0.89-0.96 for LPA replacement, HR=0.65, 0.56-0.79 for MVPA replacement). However, for the most active, substitution of sitting time with LPA or MVPA was not associated with a significant reduction in mortality risk (HR=1.00, 0.97-1.02, HR=0.97, 0.95-1.01, respectively).

Conclusions: These findings suggest that replacing modest amounts of sedentary time with even light intensity physical activities may have the potential to improve health among those failing to meet physical activity guidelines.

5.2. Introduction

Substantial evidence exists suggesting that regular physical activity is associated with a lower risk of cardiovascular disease, type II diabetes, certain types of cancer, and premature death.(1-3) It is estimated that an insufficient amount of moderate-to-vigorous physical activity (MVPA), referred to as physical inactivity, is responsible for between 6-10% of the world's burden of chronic diseases.(4) Distinct from physical inactivity, the amount of time spent engaging in sedentary behavior (characterized by very low energy expenditure (≤1.5 METs) while in a sitting, reclining, or lying position) is also associated with a higher risk of premature death and chronic disease.(5-10) This may be due, at least in part, to the displacement of physical activities with sedentary behaviors.

During waking hours, a person is either sedentary or physically active at a light, moderate, or vigorous intensity. However, even for the most active Americans, a very small portion of the day is spent on moderate or vigorous intensity activities.(11) Americans currently spend at least 7.7 waking hours/day sedentary, reflecting the high proportion of time spent on sedentary activities.(12) Because there is a finite amount of time in a day, it is necessary to consider that time spent on one active or sedentary behavior displaces time spent on another.(13) Until recently, most studies explored the associations of sedentary time and various health outcomes without considering the physical activities being displaced. This has left a gap in our understanding of healthful proportions of activity time, as it is not yet clear if sedentary time must be replaced with MVPA to be beneficial, or if replacement with light physical activity (LPA) may be similarly beneficial for both active and inactive participants.

Using isotemporal substitution models (ISM), it is possible to estimate the mortality risk reductions for replacing sedentary time with time-matched physical activities, allowing for the consideration of activities displaced and the fixed amount of discretionary time available in a day.(14, 15) While many early isotemporal substitution studies primarily used cross-sectional data to explore associations between replacing sedentary time and various metabolic outcomes, more recently prospective studies have examined the associations between the replacement of sedentary time and mortality risk.(16-18) One prospective study found significant reductions in all-cause mortality risk for substituting one hour of sitting time with one hour of walking (Hazard Ratio (HR), 95% Confidence Intervals (CI) = 0.86, 0.81-0.90) or with one hour of MVPA (HR = 0.88, 95% CI 0.85-0.90).(19) Another study found meaningful differences in risk based on participants' current level of activity.(20) For more active participants (those reporting ≥2 hours/day of total physical activity [LPA and MVPA combined]), the substitution of one hour/day of sedentary time was associated with a reduced risk for all-cause mortality when replaced with equal amounts of MVPA (HR = 0.91, 95% CI 0.88-0.94]), but there were no benefits associated with replacing one hour/day of sedentary time with one hour/day of LPA (HR = 1.0, 95% CI 0.98-1.02). On the other hand, the less active participants benefited from replacing one hour/day of sedentary time with one hour/day of LPA (HR = 0.70, 95% CI 0.66-0.74), although mortality benefits were greater when sedentary time was replaced with MVPA (HR = 0.58, 95% CI 0.54-0.63).

The primary aim of this study is to estimate the all-cause mortality risk reductions associated with replacing thirty minutes of total sedentary time with thirty minutes of either LPA or MVPA in a large prospective cohort of U.S. adults. Secondary aims include estimating: 1) the mortality risk reductions associated with replacing thirty minutes of daily sedentary time with time-matched LPA or MVPA among low, moderate, and high active participants separately, 2) associations for cancer, cardiovascular disease, and other causes of death, and 3) the mortality risk reduction stratified by sex, age group, and body mass index (BMI).

5.3. Methods

The Cancer Prevention Study-II (CPS-II) is a prospective study of cancer mortality initiated by the American Cancer Society in 1982, and includes approximately 1.2 million participants.(21) In 1992, a subset of the CPS-II participants who lived in one of 21 states were invited to join the CPS-II Nutrition Cohort (CPS-II NC).(22) The CPS-II NC, which includes over 184,000 participants between the ages of 50 and 74 years at baseline, was established to update exposure information, including health behaviors such as physical activity and sitting time. CPS-II NC participants completed a 10-page questionnaire at home and received subsequent questionnaires every two years beginning in 1997. The 1999 follow-up survey was used as the baseline for this analysis, as it included more detailed questions on physical activity and sitting time than previous surveys. All aspects of the CPS-II are approved by the Emory University Institutional Review Board.

The 151,343 men and women who completed the 1999 CPS-II NC follow-up survey were eligible for inclusion in this analysis. Participants with a history of cancer (N = 12,635), cardiovascular disease or stroke (N = 18,754), or emphysema/other lung disease (N = 3,537) at the 1999 baseline were excluded from the analysis. Participants were also excluded if they were missing survey information on physical activity (N = 3,801) or sitting time (N = 2,512), reported zero minutes of sitting time (N = 171), had a missing or extreme (top and bottom 0.1%) body mass index (N = 4,925), or were missing information on their smoking status (N = 129). To reduce the possibility of reverse causality due to undiagnosed illness or disability at baseline, participants dying within the first year of follow-up (N = 910) or reporting no LPA or MVPA were also excluded (N = 2,212). The remaining 101,757 participants were included in this analysis.

Measures

Time spent sitting was assessed with the question, “During the past year, what was your average total time per week spent at each of the following activities?” with responses including: sitting at work, sitting or driving in a car/bus/train, sitting or lying watching TV, sitting at home reading, and other sitting. Responses included: none, 1-39 min, 40-89 min, 1.5 hrs, 2-3 hrs, 4-6 hrs, 7-10 hrs, 11-20 hrs, 21-30 hrs, 31-40 hrs, or 40+ hrs The midpoint value from each sitting category (i.e., 20 min, 65 min, 1.5 hrs, 2.5 hrs, 5 hrs, 8.5 hrs, 15.5 hrs, 35.5 hrs, and 40 hrs) was summed and used to generate average daily total sitting time.

Information on leisure-time physical activity was collected with the question, “During the past year, what was your average total time per week spent at each of the following activities?”. Time spent dancing, gardening/mowing/planting, and doing low intensity exercise was used to calculate average daily minutes of LPA. Similarly, time spent walking, jogging/running, lap swimming, playing tennis or racquetball, bicycling/exercise machines, and engaging in aerobics/calisthenics was used for calculating average daily minutes of MVPA. The midpoint values from responses including: none, 1-19 min, 20-59 min, 1 hr, 1-1.5 hrs, 2-3 hrs, 4-6 hrs, 7-10 hrs, and 11+ hrs, were used to form average daily LPA and MVPA values.

The primary outcome was death ascertained through biennial linkage of the cohort with the National Death Index. (23) Causes of death were classified with the *International Classification of Diseases* (ICD), Tenth Revision for deaths occurring one year after the 1999 survey completion through 2014.(24) Death certificates or cause of death codes were obtained for 98.7% of all deaths. Deaths were grouped into four categories: all-cause, cancer, cardiovascular disease (CVD), and other causes.

Statistical Analysis

Cox proportional hazards regression modeling with an isotemporal substitution framework was used to compute hazard ratios (HR) and 95% confidence intervals (CI) for the replacement of thirty minutes of sitting time with LPA or MVPA in three models: 1) adjusted for age (stratified on year of age) and sex, 2) adjusted for age, sex, and other potential confounding factors, and 3) adjusted for age, sex, other confounding factors, and BMI (continuous, (kg/m^2)). Additional potential confounders included: race (white, black, other/unknown), alcohol use (non-drinker, <1, 1, ≥2 drinks/day), smoking status (never, current, former, unknown), years since quitting among former smokers (<10, 10-19, ≥ 20 years), cigarette frequency and smoking duration among current smokers (<20 cigarettes/day and smoking ≤35 years, <20 cigarettes/day and smoking >35 years, 20+ cigarettes/day and smoking ≤35 years, 20+ cigarettes/day and smoking >35 years), aspirin use (non-user, <15, 15-29, 30+ pills/month), education (high school or some college, college graduate or higher, unknown), occupational status (employed, not employed/retired, unknown), ACS dietary guidelines adherence score (0-<3, 3-<6, ≥6), and comorbidity score (0, 1, ≥2 comorbidities, including high blood pressure, diabetes, and high cholesterol).(25)

The ISM used in the proposed main analysis can be expressed as:

$$\text{Mortality risk}_{\text{sitting}} = (b_1)\text{ light intensity physical activities (min)} + (b_2)\text{ moderate-to-vigorous intensity activities (min)} + (b_3)\text{ total duration (min)} + (b_4)\text{ covariates,}$$

where $b_1 - b_4$ are coefficients of activities or covariates and 'total duration' is the sum of the average daily duration reported for all the sedentary and active behaviors. When one behavior (in the case of the model above, sitting time) is eliminated, the total duration coefficient represents the omitted activity component, and the remaining physical activity coefficients represent the consequence of substituting thirty minutes of that activity for the eliminated activity while holding total time and the influence of all other activities constant. (13, 14)

Secondary analyses tested for effect modification of the mortality benefits associated with the isotemporal replacement of sedentary time by MVPA level (in tertiles: low active ≤ 17 min MVPA/day, moderate active > 17 min MVPA /day and ≤ 34 min MVPA /day, high active > 34 min MVPA /day), sex, age group (<65, 65-<75, ≥75), and BMI (normal, overweight, and obese). Several sensitivity analyses were also conducted: 1) among participants who were life-long non-smokers or former smokers of more than 20 years at baseline (n=81,268), 2) among participants without physical limitations (n=101,136), 3) excluding deaths occurring within the first two years of follow-up to address the possibility of reverse causality (n=100,751), and 4) excluding participants working full- or part-time (n=83,066). Interaction terms between sitting time and follow-up time were created to test the Cox proportional hazards assumption. All statistical tests were two-sided and $p<0.05$ was considered statistically significant. Analyses were conducted using SAS v.9.4 (SAS Institute Inc., Cary, NC).

5.4. Results

During 13 years (2000-2013) of follow-up, 16,163 men and 15,638 women died. Participants reporting more MVPA had a lower average BMI, were more likely to possess college degrees, were less likely to be current smokers, and had higher ACS dietary guidelines adherence scores (Table 5.1). Total sedentary time was largely comprised of sitting or lying watching TV (39%), followed by sitting at home reading (21%).

Overall, reallocation of 30 min·day^{-1} of sitting to LPA (HR=0.94, 95% CI 0.92-0.97) or MVPA (HR=0.91, 95% CI 0.88-0.93) was associated with significant reductions in all-cause mortality risk after adjusting for potential confounders. However, there was significant variation in all-cause mortality benefits by underlying physical activity level (Figure 5.1). The most active participants did not benefit from the replacement of sedentary time with LPA. However, the replacement of sedentary time with LPA was associated with a lower mortality risk for both moderate (HR=0.91, 95% CI 0.89-0.96) and low (HR=0.86, 95% CI 0.83-0.89) active participants, although benefits were greater for both groups when sedentary time was replaced with MVPA (HR=0.65, 95% CI 0.56-0.79 for moderate active; HR=0.50, 95% CI 0.44-0.58 for low active). Results for cancer and CVD mortality were largely similar, except for small differences among the moderately active group including a non-statistically significant cancer mortality risk reduction for the allocation of sedentary time to LPA (HR=0.97, 95% CI 0.91-1.02), and lower than expected CVD benefit for allocation of sedentary time to MVPA (HR=0.89, 95% CI 0.66-1.18; Table 5.2). Estimated risks associated with reallocation of sedentary time were largest for death by other causes, highlighted by significant mortality benefits among the most active group for MVPA replacement of sedentary time (HR=0.94, 95% CI 0.91-0.98).

Given the significant interaction by underlying activity level, detailed analyses by sex, age, and BMI groups were restricted to moderate and low active participants only (Table 5.3). Results were broadly consistent when stratified on sex and BMI group. However, significant interactions by age revealed larger all-cause and other cause mortality benefits for older adults when sedentary time was replaced with LPA, a finding which was largely insignificant for adults < 65 years of age. Although not statistically significant, a similar trend by age was seen for CVD mortality.

All sensitivity analyses were stratified by PA level (Table 5.4). Restricting to never and long-term former smokers, excluding deaths occurring in the first two years of follow-up, excluding participants with physical limitations, and excluding full- and part-time workers yielded risk estimates similar to the primary results.

5.5. Discussion

In this prospective study of older U.S. adults, the isotemporal replacement of 30 min·day^{-1} of sedentary time with LPA or MVPA was associated with lower mortality from all causes. Replacement benefits varied substantially by underlying physical activity level, such that replacement of sedentary time with LPA among participants with the lowest physical activity levels was associated with an 11% reduction in cancer mortality risk, a 16% reduction in CVD mortality risk, and a 17% reduction in the risk of death by other causes. However, the same reallocation of activity time among the most active participants was not significantly associated with cancer or CVD mortality benefits. As expected, the replacement of sedentary time with MVPA resulted in larger mortality benefits for all three activity groups; the largest benefits were seen in the least active group, including a 50% all-cause mortality risk reduction with the replacement of sedentary time with MVPA.

The results of this study are broadly consistent with prior studies of isotemporal substitution of sedentary time in relation to mortality. One prospective study found similar overall reductions in all-cause mortality risk for substituting one hour of sitting time with one hour of walking (HR=0.86, 0.81-0.90) or with one hour of MVPA (HR=0.88, 0.85-0.90).(19) Meanwhile, two studies using NHANES accelerometry data found slightly lower overall all-cause mortality risk reductions for the replacement of 30 min·day^{-1} of LPA (HR=0.80, 0.75-0.85; HR=0.86, 0.83-0.90) or MVPA (HR=0.49, 0.25-0.97; HR=0.58, 0.36-0.93).(26, 27) While these isotemporal substitution studies have benefitted from the use of objectively-measured physical activity data, they have largely been unable to examine effect modification by activity level or cause-specific mortality because of relatively small sample sizes. Only one other study found meaningful differences in substitution effects based on participants' current level of activity.(20) In this study, the replacement of one hour·day^{-1} of sedentary time with one hour·day^{-1} of non-exercise physical activity (HR=0.70, 0.66-0.74) or MVPA (HR=0.58, 0.54-0.63) was highly associated with mortality among less active participants, meanwhile more active participants only benefitted when sedentary time was replaced with MVPA (HR=0.91, 0.88-0.94).

In the current study, the mortality benefits associated with the replacement of sedentary time were largest for death by all other causes. The top causes of death in the 'other' category included: dementia/Alzheimer's disease (n=2800 deaths), respiratory diseases (including COPD and pneumonia, n=1381 deaths), and Parkinson's disease (n=771 deaths). While detailed cause-specific mortality has not been explored with an isotemporal framework, one recent study found that each 2-hour/day increase in sitting while watching TV was significantly associated with an increased risk of mortality for COPD, Parkinson's, and flu/pneumonia.(10)

The findings related to the mortality benefits associated with LPA add to the rather small, conflicting body of literature on lighter intensity physical activities. A few prior studies have found a significant association between LPA and mortality (28-30) while others have found no association.(31) The methodology used in the current study allows for the consideration of the sedentary time displaced by LPA. As a result, LPA (and the displaced sedentary time) in the current study was associated with a decreased risk of death by cancer, CVD, and other causes in low active participants, and with a decreased risk of death by CVD and other causes in the moderately active participants. This finding is relevant to public health as LPA may be more attainable for certain groups failing to meet physical activity guidelines, including older adults. In fact, the significant interaction by age in this study suggests that older adults may benefit more from the allocation of sedentary time to LPA.

The strengths of this study include the prospective design with 13 years of follow-up, a large sample size, the ability to control for several potential confounders, and the use of a relatively novel statistical approach which allows for the consideration of activities displaced by sedentary time. This study may be limited by the reliance on self-reported physical activity and sitting time data. One specific limitation of the 1999 CPS-II NC survey is the lack of information on certain activities of daily living, such as cleaning, self-care, cooking, or child/older adult care. As these ADLs are particularly common for older adults, light physical activity time may be underestimated in this analysis. Similarly, this survey does not include items regarding sleep quantity, and although this information is not required for an isotemporal substitution analysis, it would indeed add to the sparse literature on healthful proportions of sleep, sedentary, and active time. Finally, given the lack of vigorous physical activity reported by adults in this cohort, it was not possible to compare the replacement of sedentary time with moderate vs. vigorous intensity physical activities.

Conclusions

Among the least active and moderately active, the reallocation of 30 min·day^{-1} of sitting time with 30 min·day^{-1} of LPA or MVPA was associated with longevity, although the associations were strongest when sitting time was replaced with MVPA. These findings suggest that replacing modest amounts of sedentary time with even lighter intensity physical activities may have the potential to improve public health among those failing to meet physical activity guidelines.

5.6. References

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Table 5.1 Baseline characteristics of CPS-II NC, 1999 Survey (n = 101,757)

	Sitting Time Level*			**Physical Activity Level****		
	High (n=34770)	Mod (n=31894)	Low (n=35093)	Low (n=48359)	Mod (n=25645)	High (n=27753)
Total sed min·day^{-1}	339 ± 114	158 ± 32	60 ± 24	162 ± 140	181 ± 131	202 ± 135
TV sed min·day^{-1}	132 ± 86	63 ± 36	22 ± 15	67 ± 75	71 ± 70	77 ± 71
Work sed min·day^{-1}	67 ± 96	15 ± 29	5 ± 11	29 ± 67	32 ± 68	30 ± 64
Transport sed min·day^{-1}	46 ± 51	27 ± 20	13 ± 10	24 ± 34	27 ± 33	33 ± 37
Home sed min·day^{-1}	62 ± 56	36 ± 26	14 ± 11	30 ± 40	36 ± 39	43 ± 43
Other sed min·day^{-1}	42 ± 55	21 ± 22	9 ± 9	21 ± 38	23 ± 36	27 ± 39
LPA min·day^{-1}	22 ± 27	22 ± 25	17 ± 22	15 ± 20	17 ± 21	25 ± 28
MVPA min·day^{-1}	40 ± 34	38 ± 32	29 ± 28	7 ± 4	20 ± 4	68 ± 6
Avg min·day^{-1} reported	401 ± 124	218 ± 56	106 ± 49	185 ± 142	218 ± 134	287 ± 146
Sex						
Male	45.9%	38.8%	35.8%	36.4%	36.3%	44.4%
Female	54.9%	61.2%	64.2%	63.6%	63.7%	55.6%
Age	68.3 ± 6.3	69.0 ± 5.9	69.8 ± 6.1	69.6 ± 6.4	69.0 ± 6.2	68.7 ± 5.9
Race/Ethnicity						
White	97.6%	97.8%	96.9%	96.9%	97.6%	97.6%
Other	2.4%	2.2%	3.1%	3.1%	2.4%	2.4%
BMI	26.7 ± 4.6	26.0 ± 4.2	26.0 ± 4.3	27.1 ± 4.9	26.3 ± 4.4	25.7 ± 4.0
Education						
Less than college grad	54.9%	57.6%	65.8%	67.0%	59.8%	54.6%
College and beyond	45.0%	42.1%	33.5%	32.4%	39.6%	44.8%
Alcoholic drinks·day^{-1}						
Non-drinker	33.9%	36.2%	39.5%	42.4%	37.9%	32.5%
<1	30.2%	31.3%	28.8%	25.9%	31.1%	31.8%
1	11.1%	11.1%	9.2%	7.2%	9.9%	12.7%
>1	9.1%	7.9%	7.1%	6.4%	7.4%	9.4%
Smoke status						
Never	46.1%	49.1%	49.6%	49.3%	49.7%	46.9%
Former	45.7%	43.8%	41.5%	40.2%	42.9%	46.1%

Current	7.3%	6.1%	7.5%	9.3%	6.3%	6.0%
Diet Score	3.9 ± 2.1	4.1 ± 2.1	4.1 ± 2.1	3.7 ± 2.0	4.0 ± 2.0	4.3 ± 2.1
Comorbidity Score	0.7 ± 0.8	0.7 ± 0.8	0.7 ± 0.8	0.7 ± 0.8	0.7 ± 0.8	0.6 ± 0.7

Values are presented as % or Mean ± SD; * Sedentary time categories split into approximate tertiles: high sitting > 218 $\text{min}\cdot\text{day}^{-1}$, medium sitting ≤ 218 $\text{min}\cdot\text{day}^{-1}$ and > 103 $\text{min}\cdot\text{day}^{-1}$, low sitting ≤ 103 $\text{min}\cdot\text{day}^{-1}$; **Physical Activity level categories split into approximate tertiles: low active ≤ 17 $\text{min}\cdot\text{day}^{-1}$, moderate active > 17 $\text{min}\cdot\text{day}^{-1}$. and ≤ $\text{min}\cdot\text{day}^{-1}$, high active > 34 $\text{min}\cdot\text{day}^{-1}$.

Table 5.2 Multivariable adjusted HR and 95% Confidence Intervals (CI) of cause-specific mortality associated with the replacement of 30 minutes of sitting time with physical activity

	Activity Level (HR (95% CI))			
	Low active	**Moderate active**	**High active**	
Cancer	**No. deaths = 4168**	**No. deaths = 2235**	**No. deaths = 2652**	***$p_{\text{int.}}$**
Model 1				
Replace with LPA	0.88 (0.83-0.94)	0.97 (0.92-1.03)	1.03 (1.00-1.06)	
Replace with MVPA	0.53 (0.41-0.70)	0.60 (0.44-0.81)	1.01 (0.95-1.03)	
Model 2				
Replace with LPA	0.89 (0.83-0.95)	0.98 (0.91-1.03)	1.03 (1.00-1.06)	
Replace with MVPA	0.60 (0.45-0.76)	0.62 (0.45-0.84)	1.00 (0.98-1.01)	
Model 3				
Replace with LPA	0.89 (0.83-0.95)	0.97 (0.91-1.02)	1.03 (1.00-1.05)	0.0087 LPA
Replace with MVPA	0.60 (0.45-0.76)	0.61 (0.45-0.86)	1.00 (0.97-1.03)	<0.0001 MVPA
CVD	**No. deaths = 4253**	**No. deaths = 2602**	**No. deaths = 3489**	
Model 1				
Replace with LPA	0.81 (0.76-0.86)	0.86 (0.81-0.91)	0.99 (0.94-1.03)	
Replace with MVPA	0.48 (0.39-0.62)	0.76 (0.56-0.99)	0.97 (0.95-1.00)	
Model 2				
Replace with LPA	0.84 (0.79-0.87)	0.88 (0.66-1.14)	1.01 (0.98-1.03)	
Replace with MVPA	0.53 (0.42-0.66)	0.87 (0.84-0.94)	0.98 (0.96-1.00)	
Model 3				
Replace with LPA	0.84 (0.79-0.89)	0.90 (0.84-0.95)	1.00 (0.98-1.04)	<0.0001 LPA
Replace with MVPA	0.55 (0.43-0.68)	0.89 (0.66-1.18)	0.98 (0.95-1.04)	<0.0001 MVPA
All other causes	**No. deaths = 5016**	**No. deaths = 3035**	**No. deaths = 4351**	
Model 1				
Replace with LPA	0.83 (0.78-0.89)	0.92 (0.86-0.98)	0.98 (0.94-1.01)	

Replace with MVPA	0.39 (0.31-0.48)	0.49 (0.37-0.64)	0.94 (0.91-0.97)	
Model 2				
Replace with LPA	0.83 (0.81-0.89)	0.94 (0.88-0.97)	0.98 (0.95-1.03)	
Replace with MVPA	0.44 (0.35-0.55)	0.55 (0.41-0.72)	0.95 (0.92-0.98)	
Model 3				
Replace with LPA	0.83 (0.79-0.89)	0.94 (0.89-0.98)	0.97 (0.93-1.01)	<0.0001 LPA
Replace with MVPA	0.43 (0.34-0.53)	0.53 (0.40-0.71)	0.94 (0.91-0.98)	<0.0001 MVPA

Model 1: adjusts for age and sex; Model 2: adjusts for age, sex, race/ethnicity, alcohol use, smoking status/freq/dur, aspirin use, education, ACS diet score, and comorbidity score; Model 3: model 2 + BMI. Activity categories split into approximate tertiles: low active ≤ 17 min·day^{-1}, moderate active > 17 min·day^{-1} and ≤ 34 min·day^{-1}, high active > min·day^{-1}. **p* value for interaction by PA category.

Table 5.3 Multivariable adjusted HR and 95% CI of cause-specific mortality associated with the replacement of 30 minutes of sitting time with physical activity among moderate and low active, stratified by sex, age, and BMI

	All-Cause HR (95% CI)	**Cancer HR (95% CI)**	**CVD HR (95% CI)**	**Other HR (95% CI)**
Men (n=19386)	**No. deaths=8541**	**No. deaths=2237**	**No. deaths=2905**	**No. deaths=3399**
Replace with LPA	0.89 (0.86-0.92)	0.94 (0.89-1.01)	0.83 (0.78-0.87)	0.90 (0.86-0.94)
Replace with MVPA	0.58 (0.53-0.64)	0.66 (0.55-0.76)	0.66 (0.56-0.74)	0.48 (0.72-0.56)
Women (n=34012)	**No. deaths=9823**	**No. deaths=2650**	**No. deaths=3186**	**No. deaths=3987**
Replace with LPA	0.89 (0.84-0.92)	0.94 (0.89-1.00)	0.86 (0.81-0.91)	0.86 (0.81-0.89)
Replace with MVPA	0.66 (0.60-0.72)	0.76 (0.66-0.89)	0.68 (0.58-0.77)	0.58 (0.51-0.65)
	*p_{int}: 0.47 LPA, 0.05 MVPA	p_{int}: 0.81 LPA, 0.18 MVPA	p_{int}: 0.64 LPA, 0.73 MVPA	p_{int}: 0.07 LPA, 0.08 MVPA
Age < 65 (n=13097)	**No. deaths=1588**	**No. deaths=761**	**No. deaths=346**	**No. deaths=481**
Replace with LPA	0.94 (0.86-1.02)	0.97 (0.86-1.06)	0.91 (0.74-1.07)	0.91 (0.79-1.06)
Replace with MVPA	0.58 (0.48-0.71)	0.68 (0.50-0.88)	0.70 (0.47-1.07)	0.41 (0.28-0.60)
Age 65-<75 (n=28441)	**No. deaths=8933**	**No. deaths=2694**	**No. deaths=2719**	**No. deaths=3520**
Replace with LPA	0.89 (0.85-0.92)	0.91 (0.86-0.98)	0.86 (0.81-0.92)	0.91 (0.86-0.97)
Replace with MVPA	0.60 (0.54-0.64)	0.70 (0.60-0.81)	0.62 (0.53-0.72)	0.50 (0.44-0.58)
Age ≥ 75 (n=11860)	**No. deaths=7843**	**No. deaths=1432**	**No. deaths=3026**	**No. deaths=3385**
Replace with LPA	0.86 (0.83-0.91)	1.00 (0.91-1.06)	0.83 (0.79-0.89)	0.83 (0.80-0.88)
Replace with MVPA	0.66 (0.60-0.71)	0.76 (0.62-0.94)	0.70 (0.60-0.80)	0.58 (0.51-0.68)
	p_{int}: 0.03 LPA, 0.42 MVPA	p_{int}: 0.46 LPA, 0.60 MVPA	p_{int}: 0.30 LPA, 0.88 MVPA	p_{int}: 0.02 LPA, 0.10 MVPA
Normal weight BMI (n=21314)	**No. deaths=7699**	**No. deaths=1885**	**No. deaths=2494**	**No. deaths=3320**
Replace with LPA	0.89 (0.86-0.91)	0.97 (0.91-1.03)	0.86 (0.81-0.92)	0.86 (0.81-0.91)
Replace with MVPA	0.56 (0.51-0.62)	0.74 (0.68-0.89)	0.60 (0.51-0.70)	0.47 (0.40-0.53)
Overweight BMI (n=21371)	**No. deaths=7113**	**No. deaths=2032**	**No. deaths=2338**	**No. deaths=2743**
Replace with LPA	0.89 (0.85-0.94)	0.91 (0.86-0.97)	0.86 (0.79-0.92)	0.91 (0.86-0.97)
Replace with MVPA	0.68 (0.61-0.74)	0.68 (0.56-0.81)	0.81 (0.70-0.94)	0.58 (0.50-0.67)
Obese BMI (n=10713)	**No. deaths=3552**	**No. deaths=970**	**No. deaths=1259**	**No. deaths=1323**
Replace with LPA	0.89 (0.83-0.94)	0.91 (0.83-1.03)	0.86 (0.79-0.97)	0.86 (0.79-0.94)
Replace with MVPA	0.64 (0.55-0.72)	0.74 (0.58-0.97)	0.62 (0.48-0.76)	0.56 (0.45-0.72)

	p_{int}: 0.91 LPA, 0.07 MVPA	p_{int}: 0.31 LPA, 0.84 MVPA	p_{int}: 0.96 LPA, 0.37 MVPA	p_{int}: 0.55 LPA, 0.05 MVPA

Models adjust for age, sex, race/ethnicity, alcohol use, smoking status/freq/dur, aspirin use, education, ACS diet score, comorbidity score, and BMI. Only moderate and low active participants included (n=74004). **p* value for interaction by sex, age group, or BMI category.

Table 5.4. Sensitivity analyses, multivariable adjusted HR and 95% CI for all-cause mortality associated with replacement of 30 minutes of sitting time with physical activity

	Activity Level (HR (95% CI))		
	Low active	**Moderate active**	**High active**
All-Cause			
Among never smokers + former smokers (>20 years since quit) (n = 81268)	**No. deaths = 7552**	**No. deaths = 5969**	**No. deaths = 10245**
Replace with LPA	0.86 (0.83-0.89)	0.92 (0.89-0.94)	0.99 (0.96-1.04)
Replace with MVPA	0.53 (0.45-0.62)	0.72 (0.60-0.86)	0.97 (0.94-1.02)
Excluding deaths in first two years of follow-up (n = 100751)	**No. deaths = 10074**	**No. deaths = 7635**	**No. deaths = 13086**
Replace with LPA	0.86 (0.83-0.89)	0.93 (0.91-0.97)	1.00 (0.98-1.02)
Replace with MVPA	0.50 (0.41-0.56)	0.66 (0.56-0.79)	1.00 (0.97-1.01)
Excluding participants with physical limitations (n = 101136)	**No. deaths = 10299**	**No. deaths = 7806**	**No. deaths = 13352**
Replace with LPA	0.86 (0.82-0.89)	0.94 (0.88-0.98)	1.01 (0.96-1.05)
Replace with MVPA	0.51 (0.45-0.60)	0.66 (0.56-0.79)	0.97 (0.95-1.01)
Excluding participants working full- or part-time (n = 83066)	**No. deaths = 9429**	**No. deaths = 7015**	**No. deaths = 11919**
Replace with LPA	0.83 (0.81-0.86)	0.91 (0.88-0.97)	1.01 (0.98-1.03)
Replace with MVPA	0.50 (0.43-0.56)	0.70 (0.58-0.83)	0.98 (0.96-1.01)
Cancer			
Among never smokers + former smokers	**No. deaths = 1731**	**No. deaths = 1590**	**No. deaths = 2965**
Replace with LPA	0.94 (0.88-1.03)	0.95 (0.89-1.03)	0.97 (0.94-1.01)
Replace with MVPA	0.66 (0.47-0.91)	0.79 (0.54-1.13)	1.03 (1.00-1.06)
Excluding deaths in first two years of follow-up	**No. deaths = 2508**	**No. deaths = 2142**	**No. deaths = 4021**
Replace with LPA	0.91 (0.86-0.99)	1.00 (0.94-1.06)	1.03 (1.00-1.06)
Replace with MVPA	0.58 (0.44-0.76)	0.60 (0.44-0.83)	1.00 (0.97-1.03)
Excluding participants with physical limitations	**No. deaths = 2617**	**No. deaths = 2221**	**No. deaths = 4150**
Replace with LPA	0.91 (0.86-0.97)	0.97 (0.92-1.03)	1.00 (0.97-1.03)

Replace with MVPA	0.62 (0.47-0.79)	0.62 (0.45-0.83)	1.01 (0.99-1.05)
Excluding participants working full- or part-time	**No. deaths = 2222**	**No. deaths = 1898**	**No. deaths = 3550**
Replace with LPA	0.89 (0.83-0.94)	0.97 (0.91-1.03)	1.03 (1.00-1.06)
Replace with MVPA	0.55 (0.40-0.72)	0.64 (0.45-0.88)	1.00 (0.98-1.04)
CVD			
Among never smokers + former smokers	**No. deaths = 2582**	**No. deaths = 2011**	**No. deaths = 3354**
Replace with LPA	0.83 (0.76-0.90)	0.91 (0.83-0.97)	1.00 (0.97-1.03)
Replace with MVPA	0.56 (0.43-0.74)	0.89 (0.64-1.22)	1.00 (0.97-1.03)
Excluding deaths in first two years of follow-up	**No. deaths = 3346**	**No. deaths = 2517**	**No. deaths = 4137**
Replace with LPA	0.83 (0.78-0.89)	0.89 (0.83-0.94)	1.00 (0.97-1.03)
Replace with MVPA	0.51 (0.41-0.66)	0.88 (0.68-1.19)	0.99 (0.94-1.02)
Excluding participants with physical limitations	**No. deaths = 3426**	**No. deaths = 2582**	**No. deaths = 4230**
Replace with LPA	0.83 (0.79-0.89)	0.89 (0.82-0.94)	1.01 (0.97-1.04)
Replace with MVPA	0.54 (0.43-0.70)	0.91 (0.68-1.20)	0.98 (0.95-1.03)
Excluding participants working full- or part-time	**No. deaths = 3191**	**No. deaths = 2367**	**No. deaths = 3861**
Replace with LPA	0.81 (0.76-0.87)	0.88 (0.84-0.94)	1.00 (0.97-1.04)
Replace with MVPA	0.55 (0.42-0.70)	0.94 (0.69-1.29)	0.97 (0.92-1.03)
Other			
Among never smokers + former smokers	**No. deaths = 3239**	**No. deaths = 2368**	**No. deaths = 3926**
Replace with LPA	0.84 (0.78-0.89)	0.91 (0.86-0.97)	0.97 (0.93-1.01)
Replace with MVPA	0.47 (0.38-0.60)	0.56 (0.42-0.79)	0.94 (0.91-1.00)
Excluding deaths in first two years of follow-up	**No. deaths = 4220**	**No. deaths = 2976**	**No. deaths = 4928**
Replace with LPA	0.83 (0.80-0.89)	0.94 (0.88-1.00)	0.97 (0.93-1.01)
Replace with MVPA	0.43 (0.34-0.53)	0.55 (0.42-0.72)	0.94 (0.91-0.98)
Excluding participants with physical limitations	**No. deaths = 4256**	**No. deaths = 3003**	**No. deaths = 4972**
Replace with LPA	0.83 (0.80-0.88)	0.95 (0.89-0.98)	0.96 (0.94-1.01)
Replace with MVPA	0.45 (0.37-0.56)	0.53 (0.40-0.70)	0.94 (0.90-0.97)
Excluding participants working full- or part-time	**No. deaths = 4016**	**No. deaths = 2750**	**No. deaths = 4508**
Replace with LPA	0.84 (0.79-0.86)	0.91 (0.86-0.97)	0.97 (0.94-1.01)
Replace with MVPA	0.43 (0.34-0.55)	0.54 (0.41-0.74)	0.95 (0.91-0.98)

Models adjust for age, sex, race/ethnicity, alcohol use, smoking status/freq/dur, aspirin use, education, ACS diet score, comorbidity score, and BMI. Activity categories split into approximate tertiles: low active ≤ 17 min·day^{-1}, moderate active > 17 min·day^{-1} and ≤ 34 min·day^{-1}, high active > 34 min·day^{-1}.

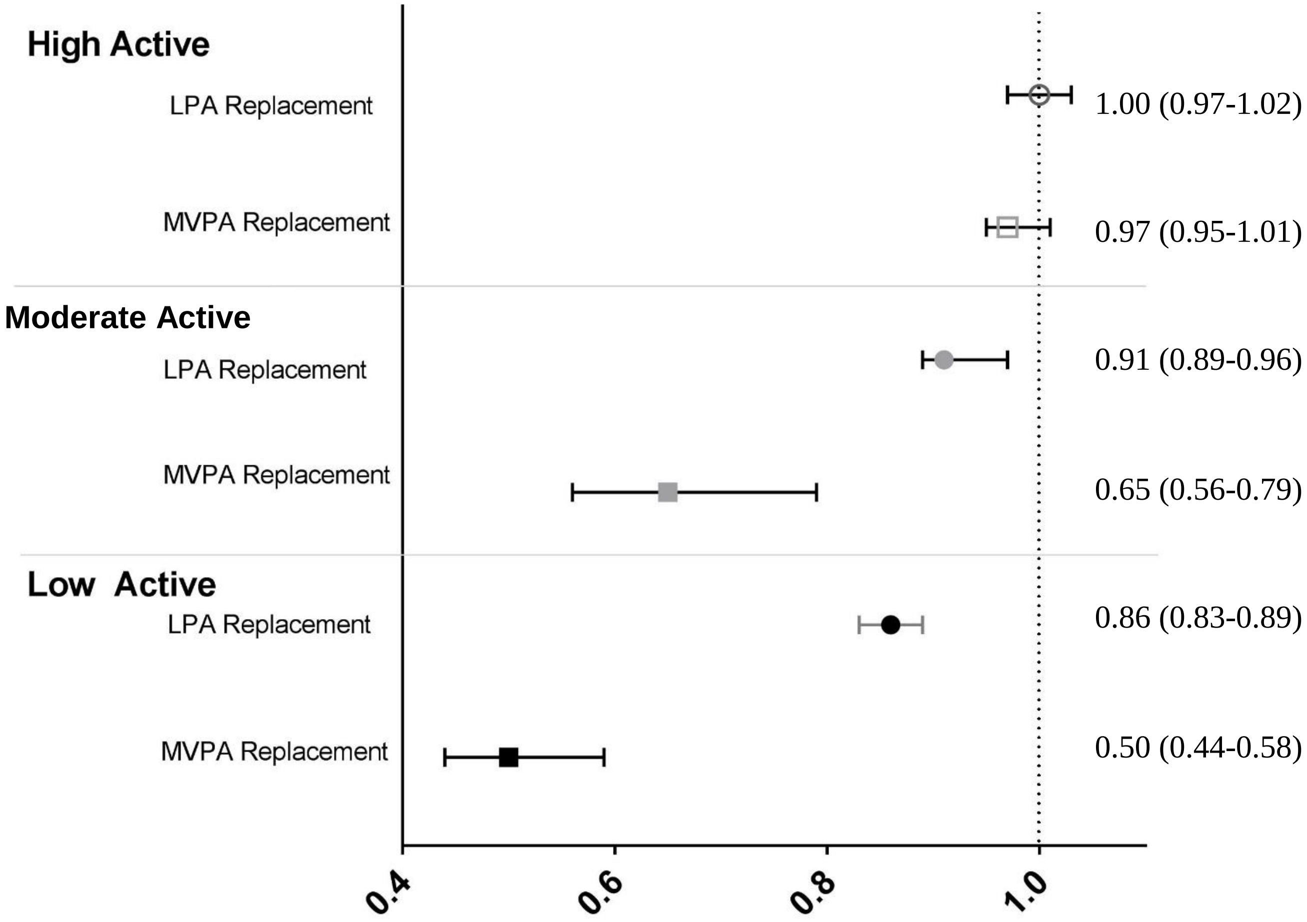

Figure 5.1. Estimated risk (HR (95% CI)) for all-cause mortality associated with replacement of 30 minutes of sitting time with physical activity. Models adjust for age, sex, race/ethnicity, alcohol use, smoking status/freq/dur, aspirin use, education, ACS diet score, comorbidity score, and BMI. Activity categories split into approximate tertiles: low active ≤ 17 min·day^{-1}, moderate active > 17 min·day^{-1} and ≤ 34 min·day^{-1}, high active > 34 min·day^{-1}.

CHAPTER 6

SUMMARY AND CONCLUSIONS

Most of the evidence for the associations of physical activity (PA), sedentary behavior (SED), and premature mortality comes from large, prospective epidemiological studies. For practical reasons regarding costs and participant and researcher burden, many epidemiological studies have relied on self-reported measures of PA and SED. However, PA and SED survey responses may be influenced by participant comprehension, trouble recalling events, social desirability bias, and other sources of random and systematic error. Given this potential for bias, it is important to conduct validation studies of PA and SED surveys.

The current validation studies suggest that the CPS-3 questionnaire has acceptable reliability and validity for ranking or categorizing participants according to PA or SED level. These findings further suggest that participant responses are not systematically biased by demographic sub-group, a finding many prior validation studies may have been too underpowered to detect. These findings are important as it is expected that CPS-3 data will provide novel information about PA, SED, and chronic disease in the future, and the presence and strength of associations observed in epidemiologic studies are a function of measure validity. Further, as the large and diverse CPS-3 cohort is a model for other studies, outside cohorts (such as the Kaiser Research Bank) have adapted and may continue to use this survey within their studies. As newer epidemiologic cohorts collect PA and SED data, utilization of the CPS-3 instrument would not only facilitate high-quality data collection, but would also allow for future harmonization or pooling of data across studies.

The PA validity study also informed future CPS-3 survey structure. By stratifying on reported walking time, it was confirmed that the lower than expected validity coefficients for the abbreviated PA grid were partially due to the inability to determine the PA intensity of walking. As a result, future CPS-3 abbreviated PA grids will include two walking items: "walking less than 3 mph or slower than 20 minutes per mile" and "walking 3+ mph or faster than 20 minutes per mile", so that walking intensity may be more accurately assigned.

Once PA and SED questionnaires are validated, they can be used with confidence in large epidemiologic studies, such as the current mortality study. Findings from this study suggested that, among the least active and moderately active, the reallocation of 30 $\text{min}\cdot\text{day}^{-1}$ of sitting time with 30 $\text{min}\cdot\text{day}^{-1}$ of light intensity physical activity (LPA) or moderate-to-vigorous intensity physical activity (MVPA) is associated with a decreased risk of mortality. Although the associations in this study were strongest when sitting time was replaced with MVPA, LPA may be viewed as more attainable or feasible for certain groups failing to meet PA guidelines. The findings related to the mortality benefits associated with LPA add to the rather small, conflicting body of literature on lighter intensity physical activities. The novel isotemporal substitution methodology used in the current study allows for the consideration of the sedentary time displaced by PA. As such, LPA (and the displaced sedentary time) was associated with a decreased risk of death by cancer, CVD, and other causes in low active participants, and with a decreased risk of death by CVD and other causes in the moderately active participants.

This study was also one of the first mortality studies to explore the role of BMI, age group, and activity level on the replacement benefits of SED. Only one other study found meaningful differences in replacement benefits based on participants' level of activity, which was defined as more (2+ hours/day total activity) or less (<2 hours/day total activity) active. The current study is the first to show significant interaction by age group on mortality risk, which suggested that older adults may benefit more from the allocation of sedentary time to LPA. As many older adults do not accumulate any MVPA, evidence of associated benefits for LPA has the potential to be particularly impactful. Overall, findings from the mortality study highlight the benefits of replacing sedentary time with physically active time among less active adults, even if the replacement activities are light in intensity and modest in time (~30 minutes per day).