Clinical impact of sedentary behaviors in adult survivors of acute lymphoblastic leukemia: A report from the St. Jude Lifetime Cohort Study

Carrie R. Howell, PhD[1], Carmen L. Wilson, PhD[1], Matthew J. Ehrhardt, MD, MS[1,2], Robyn E. Partin, MS[1], Sue C. Kaste, DO[2,3,4], Jennifer Q. Lanctot, PhD[1], Ching-Hon Pui, MD[2], Leslie L. Robison, PhD[1], Melissa M. Hudson, MD[1,2], and Kirsten K. Ness, PhD[1]

[1]Department of Epidemiology and Cancer Control, St. Jude Children's Research Hospital, Memphis, Tennessee

[2]Department of Oncology, St. Jude Children's Research Hospital, Memphis, Tennessee

[3]Department of Radiological Sciences, St. Jude Children's Research Hospital, Memphis, Tennessee

[4]Department of Radiology, University of Tennessee Health Science Center, Memphis, Tennessee

Abstract

Background—Sedentary behaviors are associated with poor health outcomes in the general population, but their clinical impact on adult survivors of childhood Acute Lymphoblastic Leukemia (ALL) has not been characterized. We describe prevalence of sedentary behaviors in ALL survivors and examine associations between time spent sedentary and body composition and cardiovascular disease (CVD) risk factor onset.

Methods—Participants self-reported screen time (e.g. television, computer) and activity measured by accelerometer were used to determine activity time (sedentary, light activity, and moderate or vigorous physical activity (MVPA)). Percent time spent in each activity was compared between 331 ALL survivors and 330 controls. Associations between time sedentary and body composition were evaluated in survivors using linear regression models. Cox proportional hazard models were used to examine the association between time sedentary at baseline and CVD risk factor onset during follow-up.

Results—Survivors spent 65% of time sedentary, 32% in light activity, and 2% in MVPA, compared to 67% (p=0.04), 30% (p<0.01) and 3% (p<0.01) for controls. Among survivors, percent lean body mass decreased by 1.0±0.4% (p=0.01) per 10% increase in time sedentary. Survivors who were sedentary ≥60%/day were at increased risk of high total cholesterol (hazard

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Corresponding author: Carrie R. Howell, PhD, Department of Epidemiology and Cancer Control, MS 735, St. Jude Children's Research, Hospital, 262 Danny Thomas Place, Memphis, TN 38105, carrie.howell@stjude.org; Phone: (901) 595-3436.

ratio [HR]: 2.52, 95% Confidence interval [CI]: 1.12–5.64) and any CVD risk factor (HR: 1.96, 95% CI: 1.16–3.30).

Conclusion—Sedentary behavior is associated with low lean mass and CVD risk factor development and should be limited in childhood ALL survivors.

INTRODUCTION

With 5-year survival rates of childhood acute lymphoblastic leukemia (ALL) close to 90% in the US,[1] long-term follow-up of survivors is important. Childhood ALL survivors are at increased risk for late onset chronic health conditions such as obesity,[2] diabetes[3] and sarcopenia,[4] which contribute to morbidity and early mortality. Understanding factors that accelerate chronic condition onset may provide information that can help to ameliorate adverse outcomes as survivors age.

Sedentary behavior, defined as energy expenditure 1.5 metabolic equivalents (METS) while in a sitting or reclined position,[5] is ubiquitous in modern society, with adults spending 6–8 hours per day on average being sedentary.[6] This is cause for concern as research demonstrates associations between sedentary and screen time behavior and poor health outcomes such as all-cause and cardiovascular disease (CVD) related mortality,[7] obesity[7], sarcopenia,[8] and cancer[7]. Among adult cancers survivors, sedentary behavior has been associated with increased weight[9] and waist circumference,[10] and CVD risk.[11]

Previous research indicates that childhood cancer survivors are sedentary[12] and that sedentary behavior in survivors is associated with abnormal bone mineral density[13] and increased risk for early CVD correlates.[14] However, previous studies used self-reported sedentary behavior measures or had small sample sizes. In light of emerging research documenting detrimental effects of sedentary behaviors on health,[7] there is a need to better characterize sedentary behaviors among childhood cancer survivors and to understand how this behavior impacts future health in the context of survivorship.

Therefore, we aimed to (1) describe sedentary and physical activity behaviors in adult childhood ALL survivors and compare to a community comparison group; (2) examine the association between sedentary and screen time behavior and body composition outcomes; and (3) examine the association between increased sedentary behavior and new onset (or increase in severity) of cardiovascular risk factors in survivors.

METHODS

Participants

Participants were members of the St. Jude Lifetime Cohort (SJLIFE), a study designed to ascertain health outcomes among adult survivors of pediatric cancer.[15] To be eligible for this ancillary study,[16] survivors had to be treated for ALL at St. Jude Children's Research

Hospital (SJCRH), survived at least 10 years since diagnosis, 18 years at SJLIFE enrollment, and not currently receiving treatment for cancer. ALL survivors diagnosed between 1980 and 2003 (N=899) and treated at SJCRH were stratified by gender, time since diagnosis, and cranial radiation exposure, and randomly recruited within strata to ensure a representative sample. When study accrual was reached (N=365), 416 ALL survivors had been approached; 51 declined (88% participation rate). An additional 35 who wore their accelerometer <3 days were excluded, leaving 330 survivors for analysis.

A community comparison group (controls) was recruited from a random sample of non-first degree family members, distant relatives and friends of current SJCRH patients and matched to a survivor based on sex, age range and race. Among 451 potential controls, 86 declined, 365 agreed to participate (81%) and 34 were excluded because of <3 days of accelerometer wear. All participants gave written informed consent prior to study participation and the protocol was approved by the SJCRH Institutional Review Board.

Sedentary and Physical Activity Behaviors

Sedentary and physical activity behaviors were assessed using physical activity monitors at baseline (first SJLIFE study visit; visits for this analysis occurred between July 2009 and December 2012). Participants were assigned a triaxial accelerometer (wGT3X-BT; ActiGraph, Pensacola FL), programmed to collect 60 second epochs, and instructed to wear for 7 days. Sedentary behavior was defined as <100 counts per minute (CPM), light activity as 100 to 1951 CPM, and moderate and vigorous physical activity (MVPA) as 1952 CPM. For the analysis of the association between sedentary time and CVD risk, we classified persons as sedentary if they met or exceeded the reported US population mean of 60%.[6]

Screen Time

At baseline only, participants were asked to indicate hours per day spent sitting and watching TV or using a computer outside of work over the last 30 days. Responses were collapsed into three categories: 2 hours, 3 to 4 hours and 5 hours.

Body Composition

Height was measured using a stadiometer (SECA, Hanover, MD) and recorded in centimeters (cm). Weight was measured using an electronic scale (Scale-tronix, White Plains, NY) and recorded in kg. Waist circumference was obtained using a Gulick tape measure, measured midway between the anterior superior iliac spine and the lower rib margin and recorded to the nearest 0.1 cm. Body mass index (BMI) was calculated by dividing weight in kg by height in meters squared. Waist to height ratio (WHtR) was calculated by dividing waist circumference in cm by height in cm. Percent lean mass was used to characterize muscle wasting as previous data have indicated associations between sedentary time and frailty,[17] of which low lean mass is a component. Percent lean mass was assessed using dual x-ray absorptiometry (DXA) (QDR4500, software version 13.3:3; Hologic, Bedford, MA) and derived by dividing fat free mass in kg by total mass in kg.

Cardiovascular Risk Factors

Cardiovascular risk factors included hypertension, high cholesterol, hypertriglyceridemia, obesity, and abnormal glucose metabolism, obtained from clinical and laboratory testing, and graded according to a modified version of the National Cancer Institute's Common Terminology Criteria for Adverse Events (CTCAE) v4.03,[18] with higher grades indicating more severe conditions. Cardiovascular risk factors were graded for survivors at baseline and at follow-up visits for those returning after baseline (n=201; June 30, 2016). Participants had the condition if they were grade 2 for hypertension (systolic resting blood pressure 140 mmHg or diastolic resting blood pressure 90 mmHg or medical intervention initiated); grade 3 for obesity (BMI 30 kg/m^2); and grade 1 for high total cholesterol (total cholesterol >300 mg/dl or on medication), hypertriglyceridemia (triglycerides >300 mg/dl or on medication), and abnormal glucose metabolism (impaired fasting glucose, insulin resistance with impaired glucose tolerance, or diabetes mellitus diagnosis).

Demographics and Health Behaviors

Participants completed questionnaires collecting demographic information and health behaviors. Educational attainment was dichotomized into having a college degree or no college degree. Participants who smoked 100 cigarettes in their lifetime were categorized as ever smoker. For males, risky drinking was defined as having >4 drinks/day or >14 drinks/week and, for females, as >3 drinks/day or >7 drinks/week.[19]

Statistics

Descriptive statistics were calculated for demographic and body composition measures and compared between groups using two-sample t-tests and chi-square tests. Generalized linear models were used to examine mean differences between survivors and controls in percent time sedentary and physically active, adjusting for demographic variables significantly different at p<0.10 in bivariate analysis: educational attainment, risky drinking, and BMI. Multivariable linear regression was used to examine the association between percent time sedentary and BMI, waist circumference, WHtR and percent lean mass, controlling for sex, age, educational attainment and cranial radiation (survivors). Multivariable linear regression was used to examine the association between screen time category and body composition outcomes, controlling for covariates mentioned above. Cox proportional hazards regression was used to evaluate the association between sedentary behavior at baseline and new onset (or increase in severity) of cardiovascular risk factors at follow-up, with time from baseline visit to cardiovascular risk factor onset or censor date (June 30, 2016) as the time scale. Hazard ratios and 95% confidence intervals were calculated for cardiovascular risk factors separately, adjusting for age, sex, the presence of each condition at baseline, and baseline MVPA minutes/day. SAS version 9.4 (SAS Institute, Inc, Cary, North Carolina) was used to conduct all analyses.

RESULTS

Both groups had a mean age of approximately 29 (survivors=28.9 [SD 6.05]; controls=29.2 [SD 7.57]); 87% were white. Survivors had less college graduates than controls (34.2% vs. 43.8%, p=0.01), more unemployed individuals (22.4% vs. 16.6%, p=0.10), and less risky

drinkers (41.5% vs. 50.2%, p=0.02). Survivors and controls did not differ in terms of household income (p=0.26) or geographic region (p=0.17). Among survivors, 71% spent ≥60% of their day sedentary versus 77% of controls (p=0.06). Survivors also had less favorable WHtR, waist circumference, and mean percent lean mass than controls (p's<0.01).

Sedentary, Physical Activity and Screen Time Behaviors – Survivors vs Comparison Group (Table 2)

The mean percent time spent sedentary per day was 65% among survivors compared to 67% in controls (p=0.04). Survivors also engaged more in light activity than controls (31.8% vs 29.8%, p<0.01). In contrast, survivors spent less time engaged in MVPA than controls (2.5% vs 3.0%, p<0.01). There was no difference in self-reported screen time between survivors and controls (p=0.07, Table 1).

Association between sedentary/screen time and body composition among survivors and controls

For each 10% percent increase in time spent sedentary per day in survivors (Table 3), percent lean mass decreased by 1.0% (p=0.01). Percent time spent sedentary was not associated with BMI, waist circumference, or WHtR or any body composition outcome in controls (Supplemental Table 2). Survivors who reported ≥5 hours of daily screen time had higher WHtR (p=0.03) and lower percent lean mass (p=0.04) than those who reported ≤2 hours/day. Controls who reported ≥5 hours/day had higher BMI (p=0.04), waist circumference (p=0.03), WHtR (p=0.04) and lower percent lean mass (p<0.01) than those who reported ≤2 hours/day.

Association between percent time spent sedentary and onset of cardiovascular risk factors

Mean follow-up time until CVD assessment or censor was 5.2 (SD 1.5) years. Survivors who spent ≥60% of their day sedentary had a 2.52 fold increased risk (95% CI: 1.12–5.64, p=0.02) of new onset of high total cholesterol at follow-up compared to survivors that spent <60% of their day sedentary (Table 4). Survivors who spent ≥60% of their day sedentary had a 1.96-fold increased risk (95% CI: 1.16–3.30, p=0.01) of new onset of any cardiovascular risk factor at follow-up compared to survivors that spent <60% of their day sedentary.

DISCUSSION

Overall, we found that adult survivors of childhood ALL engaged in less sedentary behavior than controls after adjusting for educational attainment, risky drinking and BMI. Although most body composition measures were not associated with sedentary time in survivors, we found that as percent time sedentary per day and hours watching television or using the computer outside of work increased, lean mass and WHtR outcomes were less favorable. Further, we found that survivors who spent ≥60% of their day sedentary were at increased risk of developing new or more severe cardiovascular risk factors.

Comparisons of sedentary behaviors between the two groups were contrary to our hypothesis that survivors would be more sedentary. Survivors had lower mean percent time

sedentary and fewer survivors were classified as sedentary 60% than controls. This difference could be because controls were more likely to have college degrees than survivors and therefore have occupations that do not require any manual labor. Survivors also receive risk-based follow-up care that includes education about physical activity. Even though survivors were less sedentary overall, patterns of sedentary behavior may differ between survivors and controls. We could not examine this in the current study. Finally, the difference between two groups is small (roughly 2%) and likely not clinically significant; survivors are as sedentary as their peers. Although survivors and controls wore their accelerometers, on average, for more than seven days, which is adequate to capture usual activity[20], accelerometers do not provide the opportunity to determine posture or prolonged sedentary time.[21] In addition, we used 60 second epochs to capture activity. Other programmed intervals may be more appropriate[22].

Survivors spent more time per day in sedentary behavior than reported in the general population (66% vs 60%, respectively),[6] but less than that reported by Walker et al in young children/adolescents with chronic diseases including survivors of brain tumors (66% vs 77%, respectively).[23] In contrast to the current study, Walker et al found no differences between survivors and controls; however, the comparison sample size was small (n=29); was heterogeneous in terms of disease; and was based on a much younger population.

Increased screen time and sedentary behavior were associated with lower percent lean mass, with a similar association described in community dwelling older adults.[8] The association found here had a modest effect; percent lean mass decreased roughly 1% per 10% increase in percent time sedentary. Using a metric from a recent study[24] where authors reported a 2.8% reduction in mortality per 1kg increase in lean mass, our survivors, with a mean lean mass of 56 kg, would see a 1.6% reduction in mortality per 1% increase (0.56 kg) in lean mass. Thus, as our survivors were sedentary on average 449 minutes/day, decreasing sedentary time 10% (45 minutes/day), translates into an increase in 0.56 kg in lean mass, potentially a 1.6% reduction in mortality. Since low lean mass has been previously reported in adult survivors of childhood cancer,[4] the additive effects of sedentary behaviors may be particularly harmful in this population. Counseling survivors already at risk of muscle wasting to limit sedentary behaviors and engage in resistance training may improve survivors lean muscle mass. The associations between screen time 5 hours/day and increased WHtR are similar in survivors and controls, and are concordant with some, but not all reports in adult cancer survivors. Colorectal cancer survivors who watched 5 hours of television/day had an increase in BMI at 2 and 3 years post diagnosis,[9] whereas sedentary time was not associated with waist circumference or BMI in breast[25] or prostate cancer survivors.[10]

We observed that survivors who spent 60% of their day sedentary had increased risk of new onset of cardiovascular risk factors, consistent with reports among the general population,[26] colorectal cancer survivors[11] and adult survivors of pediatric cancer.[14] Likewise, active adolescents in a large cardiovascular risk cohort indicated better CVD risk profiles over a six year period compared to their sedentary counterparts,[27] and sedentary adolescents in an atherosclerosis prevention study who increased physical activity over time had increases in endothelial function and decreases in intima-media thickness.[28] Although a direct biological

link between sedentary behavior and CVD has not been established, recent research suggests that sedentary behavior may result in decreased insulin sensitivity,[29] which has been associated with CVD risk.[30] Further, decrease in blood flow while in seating positions may reduce function of the vasculature system, and appears to be mitigated by physical activity.[31] We used a cut point of 60% time spent sedentary based on a population mean. This may not be the optimal cut point. However, these results provide preliminary evidence that sedentary behavior is associated with CVD risk among survivors. Since ALL survivors are at an elevated risk of metabolic syndrome,[32] health behaviors that aggravate these risks need to be addressed. Interventions designed to disrupt sedentary behavior and increase light to moderate physical activity in survivors of childhood cancer may lead to a reduction in onset of cardiovascular risk factors.

This manuscript has several strengths and limitations. First, we report time spent engaged in sedentary as well as physical activity among an adult cohort of childhood cancer survivors and examined the association between sedentary behaviors and body composition as well as cardiovascular risk factors, which to our knowledge, has not been described previously. Moreover, we were able to compare the sedentary behaviors the survivors with age-, sex- and race-matched controls. Third, we used both objective and subjective sedentary behavior measures, providing more precise estimates. Results should be considered in the context of several study limitations. First, these survivors were treated at one institution, thus results may not be generalizable to pediatric ALL survivors treated at other institutions. Second, our screen time measure was based on self-report, which may be subject to recall bias. Third, our comparison group was drawn from non-first degree family members, relatives and friends of current SJCRH patients, who are not necessarily reflective of the general population. Finally, we evaluated four different body composition outcomes and did not adjust for multiple comparisons. Results may be due to chance.

CONCLUSION

Sedentary behavior in childhood ALL survivors is associated with low lean mass and new onset of cardiovascular risk factors. Interventions to decrease sedentary time and increase physical activity should be considered to reduce risk of poor outcomes in survivors.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Table 1

Study participants characteristics

	Survivors[a]	Comparison Group	P
	N=330	N=331	
Demographics			
Age, Mean (SD)	28.85 (6.05)	29.18 (7.57)	0.53[b]
Sex, N (%)			0.61[c]
Female	158 (47.88)	165 (49.85)	
Male	172 (52.12)	166 (50.15)	
Race, N (%)			0.71[c]
White	289 (87.58)	287 (86.71)	
Black	39 (11.82)	40 (12.08)	
Other	2 (0.61)	4 (1.21)	
Ethnicity, N (%)			0.99[c]
Hispanic	14 (4.24)	14 (4.23)	
Non-Hispanic	316 (95.76)	317 (95.77)	
College Graduate, N (%)[d]	113 (34.24)	145 (43.81)	0.01[c]
Household Income, N (%)[e]			
<40,000	126 (38.18)	130 (39.27)	0.26[c]
40,000	145 (43.94)	157 (47.43)	
Unemployed, N (%)[f]	74 (22.42)	55 (16.62)	0.10[c]
Geographic Region, N (%)			
Northeast	59 (17.88)	44 (13.29)	0.17[c]
Southeast	236 (71.52)	261 (78.85)	
Northwest	10 (3.03)	9 (2.72)	
Southwest	25 (7.58)	17 (5.14)	
Health Behaviors			
Ever Smoker, N (%)[g]	113 (34.24)	127 (38.37)	0.26[c]
Risky Drinker[h], N (%)[i]	137 (41.52)	166 (50.15)	0.02[c]
Body Composition			
BMI, Mean (SD)	28.64 (6.97)	27.63 (7.00)	0.07[b]
Waist Circumference (cm), Mean (SD)	89.67 (16.12)	86.11 (15.69)	<0.01[b]
WHtR (%), Mean (SD)	0.53 (0.09)	0.50 (0.09)	<0.01[b]
Percent lean mass, Mean (SD)	68.52 (9.10)	70.97 (9.88)	<0.01[b]
Accelerometer-Derived Variables			
Wear time (days), Mean (SD)	7.47 (1.05)	7.26 (1.06)	0.01[b]
Sedentary 60%/day, N (%)	235 (71.2%)	257 (77.6%)	0.06[c]
Self-reported Screen time[j], N (%)			
2 hours	132 (40.00)	155 (46.83)	0.07[c]

	Survivors[a]	Comparison Group	P
	N=330	N=331	
3 to 4 hours	111 (33.64)	110 (33.23)	
5 hours	83 (25.15)	61 (18.43)	

SD: standard deviation

[a]Treatment characteristics in Supplemental Table 2

[b]Two-sample t-test

[c]Chi-square

[d]Two comparison group members did not report educational attainment

[e]Fifty-nine survivors and 44 comparison group members did not report income

[f]Fourteen survivors and 10 comparison group members did not report employment status

[g]One comparison group member did not report smoking status

[h]Defined as >4 drinks/day or >14 drinks/week for males; >3 drinks/day or >7 drinks/week for females

[i]Three survivors and five comparison group members did not report drinking status

[j]Four survivors and five comparison group members did not report screen time

Table 2

Adjusted Means of Sedentary and Physical Activity Behaviors among survivors and comparison group[a]

	Survivors	Comparison Group	Difference between means	P
	Mean (95% CI)	Mean (95% CI)	Mean (95% CI)	
Sedentary Activity (<100 CPM)				
Minutes/day	449.10 (433.43–464.76)	473.35 (458.04–488.66)	−24.26 (−45.99 to −2.53)	0.03
% time spent sedentary/day	65.66 (64.60–66.72)	67.18 (66.15–68.22)	−1.52 (−2.99 to −0.05)	0.04
Light intensity (100–1951 CPM)				
Minutes/day	219.55 (210.63–228.46)	207.99 (199.27–216.70)	11.56 (−0.81 to 23.93)	0.07
% time spent in light activity/day	31.81 (30.81–32.81)	29.79 (28.81–30.77)	2.02 (0.63 to 3.41)	<0.01
MVPA (1952 CPM)				
Minutes/day	17.29 (15.55–19.04)	21.20 (19.49–22.90)	−3.90 (−6.32 to −1.48)	<0.01
% time spent in MVPA/day	2.53 (2.29–2.77)	3.03 (2.79–3.26)	−0.50 (−0.83 to −0.17)	<0.01

95% CI: 95% Confidence interval

[a]Means adjusted for educational attainment, risky drinking status, and BMI

Table 3

Multivariable linear regression showing associations between sedentary and screen time behaviors and body composition among survivors[a]

Sedentary Time Model	BMI			Waist Circumference			Waist to Height Ratio			Percent Lean Mass		
	β	SE	P	β	SE	P	β	SE	P	β	SE	P
Percent sedentary time per day, per 10% increase	0.18	0.38	0.64	0.26	0.84	0.75	<0.01	0.01	0.85	-1.01	0.40	0.01
Female vs. male	0.42	0.74	0.57	-6.63	1.64	<0.01	0.01	0.01	0.60	-10.58	0.78	<0.01
Age at assessment	0.23	0.07	<0.01	0.74	0.15	<0.01	<0.01	<0.01	<0.01	-0.13	0.07	0.06
College degree vs. no degree	-0.68	0.80	0.40	-1.30	1.77	0.47	-0.01	0.01	0.24	0.84	0.85	0.33
Cranial radiation exposure vs. none	2.78	0.80	<0.01	5.23	1.78	<0.01	0.05	0.01	<0.01	-4.76	0.85	<0.01
Screen Time[b] Model	β	SE	P	β	SE	P	β	SE	P	β	SE	P
3-4 hours screen time vs. 2 hours	-0.05	0.87	0.95	-0.04	1.93	0.98	0.01	0.01	0.48	-0.24	0.92	0.78
5 hours screen time vs. 2 hours	1.17	0.95	0.22	3.12	2.10	0.14	0.03	0.01	0.03	-2.09	1.00	0.04
Female vs. male	0.35	0.75	0.64	-6.85	1.65	<0.01	<0.01	0.01	0.68	-10.33	0.79	<0.01
Age at assessment	0.22	0.07	<0.01	0.72	0.15	<0.01	<0.01	<0.01	<0.01	-0.10	0.07	0.15
College degree vs. no degree	-0.48	0.82	0.56	-0.84	1.81	0.64	-0.01	0.01	0.45	0.32	0.86	0.71
Cranial radiation exposure vs. none	2.74	0.81	<0.01	5.08	1.79	<0.01	0.05	0.01	<0.01	-4.60	0.85	<0.01

Beta=Difference in body composition outcome as a function of each independent variable. SE=Standard error

[a] Estimates are adjusted for sex, age at assessment, educational attainment and cranial radiation exposure

[b] Screen time=hours per day spent sitting and watching TV or using a computer outside of work over last 30 days

Table 4

Hazard ratios (HR) and 95% confidence intervals for risk of new onset of cardiovascular risk factors at follow-up by percent time spent sedentary per day at baseline in N=201 survivors[a]

	Hypertension			High Total Cholesterol			Hypertriglyceridemia		
	HR	95% CI	P	HR	95% CI	P	HR	95% CI	P
Percent sedentary <60% per day	1.0			1.0			1.0		
Percent sedentary 60% per day	2.81	0.81–9.82	0.10	2.52	1.12–5.64	0.02	1.60	0.71–3.61	0.25
Age at assessment	1.01	0.94–1.09	0.73	0.99	0.94–1.05	0.77	0.98	0.93–1.04	0.56
Female vs. male	0.66	0.26–1.67	0.38	0.78	0.41–1.48	0.44	0.73	0.35–1.56	0.42
Baseline condition present vs. not present	1.29	0.43–3.84	0.65	1.17	0.62–2.24	0.63	1.75	0.81–3.75	0.15
MVPA minutes/day	0.99	0.96–1.03	0.75	1.03	1.00–1.05	0.03	1.01	0.98–1.04	0.63

	Obesity			Abnormal Glucose Metabolism			Any Cardiovascular risk factor		
	HR	95% CI	P	HR	95% CI	P	HR	95% CI	P
Percent sedentary <60% per day	1.0			1.0			1.0		
Percent sedentary 60% per day	2.49	0.52–11.87	0.25	1.22	0.12–12.14	0.87	1.96	1.16–3.30	0.01
Age at assessment	0.92	0.82–1.02	0.11	0.91	0.75–1.10	0.33	0.99	0.95–1.03	0.52
Female vs. male	1.98	0.61–6.45	0.26	2.94	0.28–31.31	0.37	1.02	0.66–1.56	0.94
Baseline condition present vs. not present	0.97	0.29–3.28	0.96	9.84	0.92–105.33	0.06	1.59	0.95–2.66	0.07
MVPA minutes/day	1.00	0.95–1.05	0.94	0.99	0.87–1.11	0.80	1.01	0.99–1.03	0.51

[a] Hazard Ratios adjusted for age, sex, minutes of moderate to vigorous physical activity per day and presence of model specific condition at baseline (e.g. hypertension model was adjusted for presence of hypertension at baseline)