Intensity and temporal patterns of physical activity and cardiovascular disease risk in midlife

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ABSTRACT

Physical activity (PA) and sedentary time (SED) are associated with the risk of cardiovascular disease (CVD), but the temporal patterns of these behaviors most beneficial for cardiovascular health remain unknown. We aimed to identify the intensity and temporal patterns of PA and SED measured continuously by an accelerometer and their relationship with CVD risk.

At the age of 46 years, 4582 members (1916 men; 2666 women) of the Northern Finland Birth Cohort 1966 study underwent continuous measurement of PA with Polar Active (Polar Electro, Finland) accelerometers for one week. X-means clustering was applied based on 10 min average MET (metabolic equivalent) values during the measurement period. Ten-year risk of CVD was estimated using the Framingham risk model.

Most of the participants had low risk for CVD. Four distinct PA clusters were identified that were well differentiable by the intensity and temporal patterns of activity (inactive, evening active, moderately active, very active). A significant difference in 10-year CVD risk across the clusters was found in men ($p = 0.028$) and women ($p < 0.001$). Higher levels of HDL cholesterol were found in more active clusters compared to less active clusters ($p < 0.001$) in both genders. In women total cholesterol was lower in the moderately active cluster compared to the inactive and evening active clusters ($p = 0.001$).

Four distinct PA clusters were recognized based on accelerometer data and X-means clustering. A significant difference in CVD risk across the clusters was found in both genders. These results can be used in developing and promoting CVD prevention strategies.

1. Introduction[1]

Cardiovascular diseases (CVD) are a group of detrimental pathologies in the heart and vascular system. A leading cause of death, CVD causes around 30% of all deaths worldwide (World Health Organization, n.d.). Major risk factors for CVD include high blood

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[1] PA: Physical Activity, SED: Sedentary time, CVD: Cardiovascular Disease, MET: Metabolic Equivalent of a Task, BP: blood pressure, MVPA: Moderate to Vigorous Physical Activity, BMI: body mass index, R: Pearson correlation coefficient, LDL: Low-Density Lipoprotein, HDL: High-Density Lipoprotein, SBP: Systolic Blood Pressure, DBP: Diastolic Blood Pressure, ANOVA: Analysis Of Variance, CI: Confidence Interval, SD: Standard Deviation, NFBC66: The Northern Finland Birth Cohort 1966 Study.

pressure (BP), diabetes, dyslipidemia, physical inactivity, and smoking (World Health Organization, n.d.; Lowe et al., 1998; Yusuf et al., 2004). Physical activity (PA) decreases the risk of CVD (Kohl III, 2001), and even low levels of PA have been found to be associated with lower CVD risk compared to total inactivity (Lachman et al., 2018). Sedentary time (SED) has a positive, independent, and dose-response association with CVD risk regardless of the total activity level (Carter et al., 2017; Katzmarzyk et al., 2009). Negative changes in traditional CVD risk factors (blood pressure, high density lipoprotein cholesterol, glucose tolerance) in response to prolonged sitting potentially explain this association (Carter et al., 2017).

Recently, the objective measurement of PA using pedometers and accelerometers has become more feasible and accessible in large-scale studies to obtain intensity levels of PA, for example, moderate to vigorous PA (MVPA), light PA, and SED (Westerterp, 2009; Lee and Shiroma, 2013). However, whether any single metric, such as achieving MVPA 150 min per week, is enough for categorizing an individual as active or inactive has been questioned, as the same individual who engages in a lot of MVPA may also have high SED (Thompson et al., 2015). When MVPA distribution over a week has been studied, almost similar health benefits have been found for both evenly divided exercise bouts on three or more days of the week and for one or two more intensive exercise days (in so-called weekend warriors) (O'Donovan et al., 2017). In addition, the timing and duration of different activities in a day, for example, short bouts of intensive activity (an amount not fulfilling the activity recommendations) (Metcalfe et al., 2012; Glazer et al., 2013) and short breaks in prolonged SED, contribute to health (Dunstan et al., 2011; Jefferis et al., 2014). When studying sedentary patterns among middle-aged adults, highest mortality risk was found among those with both high overall SED and high sedentary bout duration (Diaz et al., 2017).

Different physical activities accruing one day are codependent of each other due to finite time. Thus, the independent role of any activity behavior in health promotion or disease prevention has remained unknown (Maher et al., 2014; Chastin et al., 2015). Compositional analyses have become popular where the effect of PA on different health outcomes has been studied by replacing one activity with another (e.g., a certain amount of SED replaced with MVPA), using both self-reporting (Matthews et al., 2015) and accelerometer data (Buman et al., 2014) to quantify physical activity. Cross-sectional studies using statistical modeling have suggested that replacing SED especially with MVPA may decrease all-cause mortality (Matthews et al., 2015) and cardiovascular disease risk (Buman et al., 2014).

Although accelerometers measure human motion continuously, reports on temporal patterns of PA are scarce, and valuable information is underutilized (Thompson et al., 2015; Silva et al., 2017). Using latent class analysis for United States national cohort PA data Evenson et al. (2015) found 5–7 different groups with different PA patterns in terms of intensity and distribution of activity (PA volume, SED, and MVPA) between weekdays and weekends. In addition, cluster analysis has been previously used to identify physical activity patterns based on questionnaire and objective PA data (Rovniak et al., 2010; Lee et al., 2013; Fukuoka et al., 2017). Lee et al. (2013) found two distinct clusters (*active* and *less active*) based on objectively measured hourly average PA counts over two weekdays and two weekend days. In a recent study among inactive women (Fukuoka et al., 2017), three clusters were found based on raw minute-level MET-data (MET refers to metabolic equivalent of a task) collected by accelerometer over seven consecutive days (*afternoon engaged*, *morning engaged*, and *unengaged*).

Information about daily and weekly variations of PA with continuous measurements is needed for recognizing healthy PA patterns and for designing and targeting efficient interventions for possible subgroups with deleterious PA patterns. The aim of the study was to identify temporal patterns of continuously measured physical activity beneficial for cardiovascular health in a middle-aged group using cluster analysis and to study how the widely used 10-year CVD risk

model (D'Agostino et al., 2008) is associated with different PA profiles. Previously, CVD risk between PA clusters has been studied with separate risk-related parameters (Fukuoka et al., 2017). For the first time, we have evaluated CVD risk between PA clusters using a well-established risk model (D'Agostino et al., 2008) and PA data collected over seven consecutive days continuously 24 h per day. We hypothesized that the intensity and temporal pattern of physical activity are positively associated with future CVD risk.

2. Methods

2.1. Study population

The Northern Finland Birth Cohort 1966 study (Northern Finland Cohorts) included all newborns whose birth was expected in 1966 in Northern Finland ($n = 12058$ live births). The Ethical Committee of the Northern Ostrobothnia Hospital District (94/2011) in Oulu, Finland, approved the study. The subjects and their parents signed a written consent form for the study. Personal identity information was encrypted and replaced with identification codes to provide full anonymity. Since 1966, data have been collected regularly from the study participants. The most recent follow-up, when participants were 46–48 years old (hereafter referred as 46 years old), included questionnaires, laboratory tests, and objective measurement of physical activity with wrist-worn accelerometers.

2.2. Questionnaire

Postal questionnaires were sent to all participants with known addresses in 2012–2014 (response rate 67%, $n = 6851$). The questionnaires include items on health, health behavior, and social background. Education, employment status, and prevalence of diagnosed diseases were addressed, and smoking status (former, current, non-smoker) and alcohol consumption (g/day) were captured based on multiple questions about drinking and smoking habits.

2.3. Clinical examination

Participants attended clinical examinations ($n = 5852$), where trained nurses comprehensively studied their medical condition. Participants' height and weight were measured, and their BMI (body mass index) was calculated as weight (kg) divided by height squared (m^2). Participants' body fat percentage and visceral fat area (cm^2) were analyzed with bioelectrical impedance measurement InBody 720 (InBody, Seoul, Korea). A strong correlation ($R = 0.76$) has been reported between computed tomography and bioelectrical impedance measurements of visceral fat area among gastric cancer patients (Ogawa et al., 2011).

In the laboratory, venous blood samples were drawn after overnight fasting for the analysis of serum total cholesterol, low-density lipoprotein (LDL) and high-density lipoprotein (HDL) cholesterol levels, which were determined by using an enzymatic assay method (Advia 1800; Siemens Healthcare Diagnostics Inc., Tarrytown, Ny, USA). The samples were analyzed in NordLab Oulu, a testing laboratory (T113) accredited by Finnish Accreditation Service (FINAS) (EN ISO 15189). Systolic (SBP) and diastolic blood pressures (DBP) were measured three times in seated position (the two latter measurements averaged; Omron M10, Omron Healthcare, Kyoto, Japan) after 15 min of rest.

2.4. Cardiovascular disease risk model

For evaluating CVD risk, the Framingham risk model was used (D'Agostino et al., 2008). The model estimates the absolute risk over 10 years (as a percentage) of overall CVD, which includes coronary heart disease (coronary death, myocardial infraction, coronary insufficiency, and angina), cerebrovascular events (including ischemic

stroke, hemorrhagic stroke, and transient ischemic attack), peripheral artery disease (intermittent claudication), and stroke. The CVD risk score was calculated separately for women and men. Variables used in the model included age, HDL cholesterol, total cholesterol, systolic blood pressure (not treated or treated), and prevalence of smoking (yes/no) and diabetes mellitus (yes/no) (D'Agostino et al., 2008). Blood pressure treatment was based on self-reported use of drugs, and smoking status and prevalence of diabetes were self-reported. Different values in these variables yield different numbers of points, and the sum of the points can be translated to a risk of contracting cardiovascular disease in the next 10 years (from < 1% risk to over 30% risk) (D'Agostino et al., 2008). Participants reporting heart failure, coronary artery disease, or inborn heart disease were excluded from the CVD risk assessment (n = 36).

2.5. Physical activity measurement

Physical activity was objectively measured with the wrist-worn, waterproof accelerometer (Polar Active, Polar Electro Oy, Kempele Finland). The accelerometer gave no feedback to the user. Polar Active, which provides MET values every 30 s (Hautala et al., 2012), has been shown to correlate (R^2 = 0.74) with the double-labeled water technique in assessing energy expenditure during exercise training (Kinnunen et al., 2012). Participants were asked to wear Polar Active monitors 24 h per day for at least 14 days, also while sleeping, in the wrist of the non-dominant hand. Daily averages of time spent in different activity levels (very light: 1–1.99 MET, light: 2–3.49 MET, moderate: 3.5–4.99 MET, vigorous: 5–7.99 MET, and vigorous+ ≥ 8 MET) were calculated for all participants based on the intensity levels provided by the manufacturer (Jauho et al., 2015). When comparing measured PA levels under free-living environment with Polar Active and Actigraph GT3X, these intensity levels for Polar Active provided more comparable results than traditionally used limits defined using hip-worn accelerometer (SED: ≤1.5 METs, light PA: 1.51–2.99 METs, moderate PA: 3–5.99 METs, and vigorous PA: ≥ 6 METs) in most of the intensity levels when using the traditional limits for Actigraph (Leinonen et al., 2017). MVPA was assessed as all activity at least 3.5 METs, while SED was assessed as the duration of very light activity. Participants with seven consecutive days with enough PA data (wear time ≥ 600 min/day) during the measuring period, starting from the second measured day, were included in the analyses. Wear time during waking hours (min/day) was calculated as the sum of all five activity levels. The bouts of MVPA with at least 10 min of consecutive MET values at least 3.5 METs were calculated (not allowing any lower MET values in between). In addition, the amount of prolonged SED was analyzed as bouts of at least 30 min (Diaz et al., 2017) of consecutive MET values between 1 and 2 METs. Total daily duration obtained in MVPA and SED bouts are reported.

2.6. Clustering

X-means cluster analysis (Pelleg and Moore, 2000) was used to identify subgroups of people with different daily activity patterns based on the objectively measured activity data. The aim was to form groups in which the intra-cluster homogeneity is high and inter-cluster homogeneity is low (Wardlaw et al., 2005). X-means cluster analysis is an expansion of the K-means algorithm in which the desirable number of cluster centers (K) is predefined and the K-means algorithm iteratively moves the centers so that the total within-cluster variance is minimized (Hastie et al., 2008). The X-means algorithm is the more practical method when the number of clusters is not known a priori, as it efficiently defines the number of clusters automatically (Pelleg and Moore, 2000). X-means clustering decides the number of clusters based on the best-scoring centroid set.

For clustering, 10-minute averages of the original MET data (MET value for every 30 s) for the selected one-week measurement period

were calculated. Seven consecutive days with valid PA data were required to confirm that each participant had same amount of weekdays and weekend days. Thus, although some participants provided more than seven valid days, only the seven days were included in the analyses. As participants received the activity monitors on different weekdays based on their scheduled visits for clinical measurements, the MET data was reorganized temporally from Monday to Sunday. Thus, 1008 variables for each participant were used for clustering (144 for each measurement day). The decision to cluster the whole seven days was made to group each participant in one of the distinct clusters. Additionally, differences between the clusters on PA intensity and temporal patterns on weekdays and weekends are reported. The number of cluster centroids from 1 to 7 was tested. Cluster analysis was performed with Weka, version 3.8.1 (Waikato Environment for Knowledge Analysis, The University of Waikato, Hamilton, New Zealand).

2.7. Statistics

The descriptive data are presented in counts and proportions, means and standard deviations (SD) or medians, and 25th and 75th percentiles for skewed data. Univariate associations between continuous variables and clusters were analyzed with analysis of variance (ANOVA) with Tukey post hoc tests for normally distributed variables and with Kruskal–Wallis tests for skewed data. Associations between categorical variables and clusters were analyzed using the Chi-square (χ^2) test, and the Z-test with Bonferroni correction was used for post-hoc analysis.

Accelerometer-measured moderate, vigorous, and very vigorous intensity activity, MVPA, bouts of MVPA and SED, measured total cholesterol and HDL cholesterol, and CVD risk were natural-log transformed to obtain normal distribution. Non-transformed values are presented in the tables. All statistical analyses were performed with IBM SPSS Statistics for Windows, version 24.0 (IBM Corp., Armonk, USA).

3. Results

From those wearing the activity monitor (n = 5621), 4582 participants (82%) provided enough PA data. Those who did not provide valid PA data were more often men (53% vs. 42%, $p < 0.001$), had 0.41 units higher BMI (95% CI 0.07–0.74, $p = 0.018$) and 0.68 units higher fat percentage (95% CI 0.04–1.31, $p = 0.038$), consumed 2.32 (95% CI 1.08–3.56) g/day more alcohol ($p < 0.001$), were more often heavy users of alcohol (11% vs. 8%, $p < 0.001$), and smokers (23% vs. 18%, $p < 0.05$), and less often non-smokers (48% vs. 55%, $p < 0.05$) compared to participants with valid PA data.

The final cluster model included four distinct clusters. Participants were divided into the clusters as follows: cluster 1 (*inactive*, n = 1881, 41.1% of the participants with valid data), cluster 2 (*evening active*, n = 802, 17.5%), cluster 3 (*moderately active*, n = 1297, 28.3%), and cluster 4 (*very active*, n = 602, 13.1%). The characteristics of the study population are presented in Table 1 and the average durations of different activity levels in clusters in Table 2. All activity levels were significantly different between clusters, with the inactive cluster having the highest amount of SED per day and the lowest amount of MVPA compared to other clusters. The patterns were similar in women and men. The amount of MVPA was highest in the very active cluster (122 min/day), which was almost 50 min/day more than in the moderately active cluster and > 70 min/day more than in the inactive cluster. The amount of MVPA obtained in at least 10-minute bouts was notably lower, below 20 min/day in all clusters, compared to all MVPA time. Wear time of the accelerometer was significantly different between clusters, with the biggest difference, 40 min/day, occurring between the inactive and moderately active clusters. Physical activity levels in clusters are presented as z-scores in a radar chart (Fig. 1).

Daily distributions of average MET values over the seven measured

Table 1
The characteristics of the study population ($n = 4582$).

Variable	Clusters				Overall p value[*]
	Inactive ($n = 1881$)	Evening active ($n = 802$)	Moderately active ($n = 1297$)	Very active ($n = 602$)	
Height, cm	168.4 (8.9)[a,b,c]	172.2 (9.1)[d,e]	170.4 (8.9)[f]	175.4 (8.3)	$p < 0.001$
Weight, kg	77.4 (17.1)[a,c]	80.4 (17.4)[d]	76.4 (15.7)[f]	81.0 (15.1)	$p < 0.001$
BMI, kg/m²	27.2 (5.2)[b,c]	27.0 (4.9)[d]	26.2 (4.4)	26.2 (4.1)	$p < 0.001$
Body fat %					$p < 0.001$
Men	24.3 (6.9)[b,c]	23.6 (7.5)[e]	22.8 (6.9)[f]	21.1 (7.0)	
Women	34.8 (8.4)[a,b,c]	33.1 (8.2)[d,e]	31.4 (7.9)	29.9 (8.1)	
Visceral fat area, cm²					$p < 0.001$
Men	103.0 (38.5)[c]	101.9 (43.0)[e]	98.2 (37.4)	91.4 (36.8)	
Women	115.5 (44.2)[b,c]	110.2 (42.1)[d,e]	100.0 (38.5)	96.7 (38.6)	
Gender					$p < 0.001$
Men, n (%)	648 (34.4)[a,c]	394 (49.1)[d,e]	493 (38.0)[f]	381 (63.3)	
Women, n (%)	1233 (65.6)[a,c]	408 (50.9)[d,e]	804 (62.0)[f]	221 (36.7)	
Profession					$p < 0.001$
No professional education, n (%)	53 (3.0)	28 (3.8)	36 (2.9)	21 (3.7)	
Vocational/college level education, n (%)	1119 (64.1)	469 (63.8)[e]	848 (69.3)[f]	448 (79.7)	
Polytechnic/university degree, n (%)	573 (32.8)	238 (32.4)[e]	339 (27.7)[f]	93 (16.5)	
Employment status					$p < 0.001$
Employed, n (%)	1499 (85.7)[b]	627 (85.8)[d]	1144 (95.2)[f]	494 (89.3)	
Studying, n (%)	38 (2.2)	14 (1.9)	11 (0.9)	7 (1.3)	
Unemployed, n (%)	117 (6.7)[b]	43 (5.9)[d]	24 (2.0)[f]	34 (6.1)[f]	
Other, n (%)	95 (5.4)[b]	47 (6.4)[d]	23 (1.9)	18 (3.3)	
Smoking					$p < 0.001$
Non-smoker, n (%)	990 (55.5)[a]	359 (47.6)[d,e]	737 (59.5)	317 (55.7)	
Current smoker, n (%)	335 (18.8)	171 (22.7)[d,e]	195 (15.7)	81 (14.3)	
Former smoker, n (%)	458 (25.7)	224 (29.7)	307 (24.8)	171 (30.0)	
Alcohol consumption					
Alcohol consumption, g/day	4.1 (1.0–11.2)[a]	5.6 (1.2–15.1)[d]	4.1 (1.0–11.2)	4.5 (1.0–14.4)	$p < 0.001$
Heavy users (men ≥40 g/day, women ≥20 g/day), n (%)	138 (7.6)	69 (9.0)	89 (7.1)	44 (7.6)	$p = 0.482$

Values are mean (SD) or median (25th–75th percentile) if not otherwise stated, SD = standard deviation. Only significant ($p < 0.05$) pairwise comparison p values are reported: [a]inactive compared to evening active, [b]inactive compared to moderately active, [c]inactive compared to very active, [d]evening active compared to moderately active, [e]evening active compared to very active, [f]moderately active compared to very active.

[*] Pairwise comparisons were made if overall p value was significant.

days in clusters are presented in Fig. 2a, and the activity patterns during weekdays and weekend days are presented in Fig. 2b and c. The inactive and moderately active clusters had fairly similar activity patterns, most of the activities occurring between 7:00 and 19:00 h. Overall intensity of activity during waking hours differed between these two clusters. In the evening active cluster, the activity pattern had shifted in time scale, and most of the activities took place at 12:00 and 21:00. The very active cluster had the highest activity level during waking hours. Similar differences in activity patterns were present also during weekdays and weekend days when examined separately. However, a clearer peak in activities during mornings and evenings in the moderately active cluster was found on weekdays. On weekend days, activity patterns shifted in time scale in all clusters, with higher intensities occurring between 10:00 and 21:00 and the intensity of activities decreasing from morning to evening.

Of all the men 73.7% ($n = 1427$) and all the women 97.3% ($n = 2622$) had low risk ($< 10\%$) of developing CVD in the next 10 years based on the Framingham risk model. Moderate risk (10–20%) was found in 22.7% ($n = 439$) and 1.8% ($n = 69$) and high risk (over 20%) in 2.1% ($n = 69$) and 0.1% ($n = 5$) of men and women, respectively. CVD risk and CVD risk factors are presented separately for men (Table 3) and women (Table 4) in PA clusters. Significant differences in CVD risk between clusters were found both in men ($p = 0.028$) and women ($p < 0.001$). Pairwise comparisons revealed that the inactive cluster had higher CVD risk compared with the very active cluster in men ($p < 0.05$). In women, the inactive cluster had higher CVD risk compared to moderately active and very active clusters, and the evening active cluster had higher risk compared to the moderately active cluster ($p < 0.05$).

4. Discussion

For the first time, this population-based study identified the intensity and temporal patterns of objectively measured physical activity and revealed their relationship with cardiovascular disease risk using X-means cluster analysis. Based on the cluster analysis, four distinct clusters were recognized (*inactive, evening active, moderately active*, and *very active*), which differed by intensity and temporal pattern of physical activity and CVD risk.

Our results are complementary to previous studies using the K-means approach. Lee et al. (2013) found distinct clusters in terms of PA intensity and Fukuoka et al. (2017) in terms of both PA intensity and timing. When compared to clusters obtained in our study, certain similarities can be found. The inactive cluster was found in all studies and two clusters with a moderate activity level but differences in timing of activities were present in our study and in the study by Fukuoka et al. (Lee et al., 2013; Fukuoka et al., 2017). However, differences in timing of activities were clearer in their study (*afternoon engaged/morning engaged*) than in ours (*moderately active/evening active*), where no clear morning active group was distinguished. Clear differences between our study and the study by Fukuoka et al. were the absence of a very active cluster in their study and lower overall MET values. These differences were apparent, as their study population consisted of a group of inactive women (Fukuoka et al., 2017).

Statistically significant differences in CVD risk between clusters were found within both genders. However, the differences were modest, in men between *inactive* and *very active* clusters 1.2% units and in women only 0.6% units between *evening active* and *moderately active*. Clinical relevance of the CVD risk differences in clusters can be argued. Overall cardiovascular disease risk in the study population was low, and

Table 2
Activity level durations in clusters.

Variable	Clusters**												Overall p value*
	Men (n = 1916)				Women (n = 2666)				All (n = 4582)				
	Inactive (n = 648)	Evening active (n = 394)	Moderately active (n = 493)	Very active (n = 381)	Inactive (n = 1233)	Evening active (n = 408)	Moderately active (n = 804)	Very active (n = 221)	Inactive (n = 1881)	Evening active (n = 802)	Moderately active (n = 1297)	Very active (n = 602)	
Sedentary time (min/day)	699 (76)[a,b,c]	661 (91)[e]	650 (73)[f]	548 (81)	663 (77)[a,b,c]	614 (94)[e]	609 (73)[f]	510 (68)	675 (79)[a,b,c]	637 (95)[d,e]	625 (76)[f]	534 (78)	p < 0.001
Sedentary time in bouts ≥30 min (min/day)	103 (67)[a,b,c]	72 (58)[e]	66 (49)[f]	74 (60)	92 (56)[a,b,c]	62 (48)[e]	62 (41)[f]	39 (30)	96 (60)[a,b,c]	67 (53)[e]	63 (45)[f]	39 (31)	p < 0.001
Light activity (min/day)	220 (53)[a,b,c]	277 (65)[e]	277 (57)[f]	337 (64)	254 (59)[a,b,c]	319 (75)[e]	311 (63)[f]	374 (70)	242 (59)[a,b,c]	298 (73)[e]	298 (63)[f]	351 (69)	p < 0.001
Moderate activity (min/day)	34 (15)[a,b,c]	49 (22)[e]	49 (17)[f]	77 (31)	22 (10)[a,b,c]	30 (15)[e]	32 (14)[f]	47 (22)	26 (13)[a,b,c]	39 (21)[e]	38 (17)[f]	66 (32)	p < 0.001
Vigorous activity (min/day)	14 (10)[a,b,c]	18 (14)[e]	19 (13)[f]	26 (18)	21 (12)[a,b,c]	28 (14)[e]	33 (16)[f]	50 (25)	18 (12)[a,b,c]	23 (15)[d,e]	28 (16)[f]	35 (24)	p < 0.001
Very vigorous activity (min/day)	6 (6)[a,b,c]	11 (9)e	12 (10)[f]	25 (20)	3 (4)[a,b,c]	6 (7)[e]	6 (7)[f]	14 (13)	4 (5)[a,b,c]	8 (9)[e]	8 (9)[f]	21 (18)	p < 0.001
MVPA (min/day)	54 (22)[a,b,c]	78 (32)[e]	80 (25)[f]	128 (44)	45 (19)[a,b,c]	64 (26)[e]	71 (23)[f]	111 (34)	48 (21)[a,b,c]	71 (30)[d,e]	74 (24)[f]	122 (42)	p < 0.001
MVPA obtained in bouts of ≥10 min (min/day)	6 (8)[b,c]	7 (11)[e]	9 (13)[f]	14 (20)	7 (9)[b,c]	8 (10)[e]	12 (13)[f]	16 (18)	7 (9)[b,c]	8 (10)[d,e]	11 (13)[f]	15 (19)	p < 0.001
Wear time (min/day)	973 (58)[a,b,c]	1016 (63)	1006 (57)	1013 (58)	962 (57)[a,b,c]	996 (63)	995 (49)	979 (57)	966 (57)[a,b,c]	1006 (64)[d]	997 (52)[f]	987 (60)	p < 0.001

Values are mean (SD), MVPA = moderate to vigorous physical activity. Only significant (p < 0.05) pairwise comparison p values are reported: [a]inactive compared to evening active, [b]inactive compared to moderately active, [c]inactive compared to very active, [d]evening active compared to moderately active, [e]evening active compared to very active, [f]moderately active compared to very active.

* Pairwise comparisons were made if overall p value was significant.

** Comparisons between clusters are performed separately for gender subgroups and all participants.
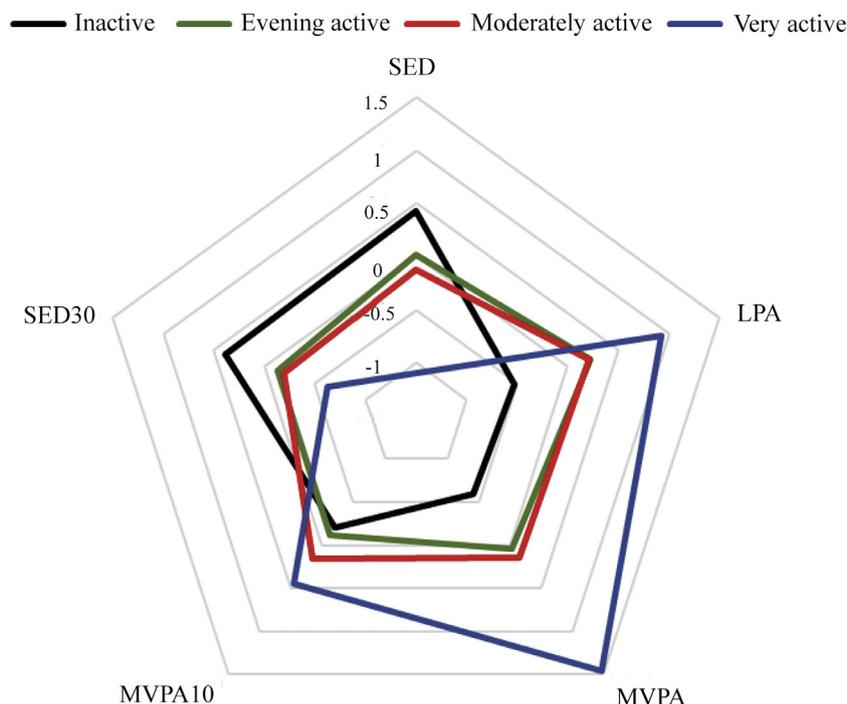
Fig. 1. Standardized cluster means (z-scores) of physical activity intensity levels in clusters.
SED sedentary time, SED30 sedentary time obtained in at least 30 min bouts, LPA light physical activity, MVPA moderate to vigorous physical activity, MVPA10 moderate to vigorous physical activity obtained in at least 10 min bouts.

notably almost all women had a lower than 10% risk of developing CVD in the next 10 years. Low CVD risk was anticipated, as the participants were relatively young. Prevalence of CVD increases considerably in men around 60–65 years of age and in women even later on (Yazdanyar and Newman, 2009). Thus, at the age of 46 years, the 10-year CVD risk will probably not yet clearly separate those at high risk later in life.

CVD risk in our study was lower compared to a recent study (Vasankari et al., 2017) using the same CVD risk model and multiple objectively measured PA variables in a Finnish population-based sample of adults (mean age 53 years, age range 18–85 years). The study reported low risk in 63%, moderate in 21%, and high risk (or already CVD) in 16% of the participants. Our study had substantially fewer of those with high risk and more of those with low risk. This discrepancy might be due to the wide age range of the participants in the previous study. We also excluded from the analyses the 36 participants who already had CVD, which might lower the risk levels in our study.

Significant differences in some of the variables included in the CVD risk model were found between the clusters. In both genders, HDL cholesterol was higher in more active clusters compared to less active. In women, total cholesterol was higher in *inactive* and *evening active* clusters compared to *moderately* and *very active* clusters. Overall, mean HDL values were above the minimum recommendation, and total cholesterol was on average slightly above to the recommended maximum level based on current national guidelines (Working group set up by the Finnish Medical Society Duodecim and the Finnish Cardiac Society, 2017) in both genders and in all PA clusters. The *evening active* cluster had the highest prevalence of smoking in both genders. There was no difference in other variables included in the Framingham score, SBP and prevalence of diabetes, between the PA clusters. Due to the birth cohort setting, the age of the participants was almost similar and led to constant CVD risk points concerning age. Systolic blood pressure with and without blood pressure medication was normal or slightly elevated in all clusters based on guidelines (Working group set up by the Finnish Medical Society Duodecim and the Finnish Cardiac Society, 2014). These results are in line with the study by Fukuoka et al. (2017), who also studied the cardiometabolic risk in clusters but did not use a

distinct risk model. They reported no significant differences between HDL, total cholesterol, and SBP between clusters with a slightly higher mean age of the sample, 52 years, compared to our study (Fukuoka et al., 2017).

4.1. Study limitations and strengths

The strengths of the study include the large population-based birth cohort design, objective continuous measurement of physical activity, and the use of a novel clustering method in analyzing the different PA behaviors and patterns over seven consecutive days. Nevertheless, the study has some limitations. Causal interactions cannot be concluded due to the cross-sectional study design. Those participants providing valid PA data seemed to have more preferable body composition, to smoke less, and to consume less alcohol compared to those with no valid PA data, which might induce selection bias and distort the population-level variation in PA values. However, compliance with wearing the accelerometer was high. Another limitation is the lack of posture recognition due to monitor placement on the wrist and thus in this work it was not possible reliably distinguish between sitting and standing postures, although their physiological responses to health can be different (Katzmarzyk, 2014). The cluster analysis did not utilize the intensity level limits provided by the manufacturer. However in describing the amount of PA these intensity levels were presented and it is notable that the activity monitor might overestimate the amount of vigorous and very vigorous PA (here defined as ≥ 5 METs) (Leinonen et al., 2017).

5. Conclusions

This study for the first time presents X-means cluster analysis with objectively measured PA data in a wide population-based sample of middle-aged people. Four distinct clusters, *inactive*, *evening active*, *moderately active*, and *very active*, were recognized. Significant differences in demographics, PA intensity levels, and CVD risk between clusters were found, and overall, more preferable levels of cholesterol
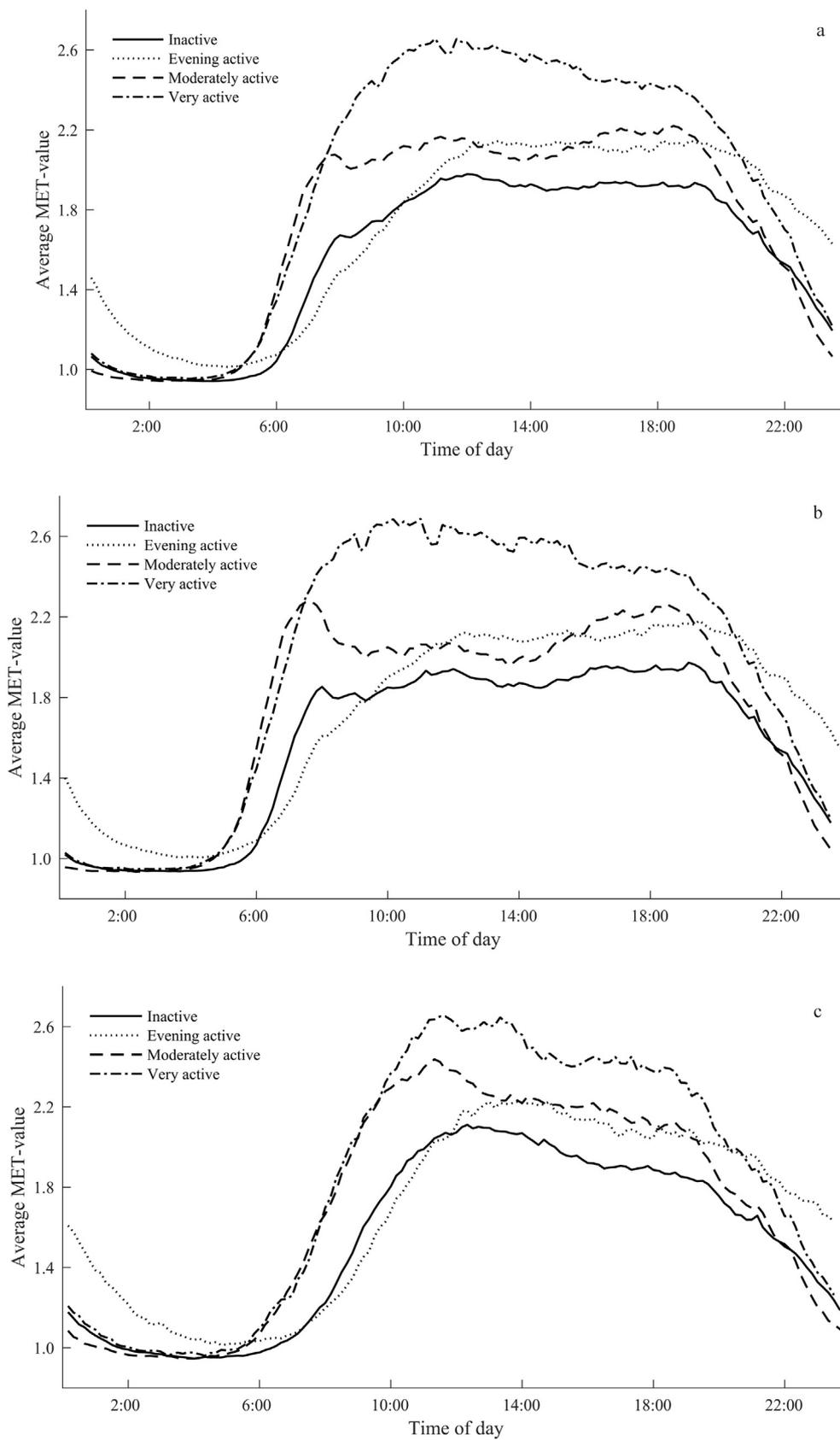
Fig. 2. Average MET-values over a) seven days, b) weekdays, c) weekend days in the activity clusters.

Table 3

Ten-year cardiovascular disease risk based on Framingham risk model and risk factors in men ($n = 1469$).

Variable	Inactive ($n = 487$)	Evening active ($n = 305$)	Moderately active ($n = 376$)	Very active ($n = 301$)	Overall p value*
CVD risk, %	8.81 (5.39)[c]	8.46 (4.70)	8.05 (4.07)	7.58 (3.84)	$p = 0.028$
HDL cholesterol, mmol/l	1.38 (0.34)[c]	1.42 (0.35)	1.41 (0.34)[f]	1.48 (0.35)	$p < 0.001$
Total cholesterol, mmol/l	5.52 (1.01)	5.56 (0.96)	5.47 (0.97)	5.58 (0.99)	$p = 0.152$
SBP not treated, mmHg	126.5 (14.6)	127.5 (13.8)	127.9 (13.5)	128.1 (12.5)	$p = 0.285$
SBP treated, mmHg	132.7 (14.1)	129.3 (11.5)	131.2 (12.3)	133.5 (14.9)	$p = 0.638$
Smoker, n (%)	108 (22.2)[c]	74 (24.3)[e]	74 (19.7)	38 (12.6)	$p = 0.002$
Diabetic, n (%)	17 (3.5)	11 (3.6)	12 (3.2)	11 (3.7)	$p = 0.987$

Values are mean (SD) if not otherwise stated, CVD = cardiovascular disease, HDL = high density lipoprotein, SBP = systolic blood pressure, SD = standard deviation. Only significant ($p < 0.05$) pairwise comparison p values are reported: [a]inactive compared to evening active, [b]inactive compared to moderately active, [c]inactive compared to very active, [d]evening active compared to moderately active, [e]evening active compared to very active, [f]moderately active compared to very active.

* Pairwise comparisons were made if overall p value was significant.

Table 4

Ten-year cardiovascular disease risk based on Framingham risk model and risk factors in women ($n = 2228$).

Variable	Inactive ($n = 1005$)	Evening active ($n = 336$)	Moderately active ($n = 705$)	Very active ($n = 182$)	Overall p value*
CVD risk, %	3.50 (2.42)[b,c]	3.57 (2.77)[d]	2.99 (1.77)	3.06 (1.93)	$p < 0.001$
HDL cholesterol, mmol/l	1.66 (0.39)[b,c]	1.67 (0.38)[d]	1.71 (0.37)[f]	1.81 (0.41)	$p < 0.001$
Total cholesterol, mmol/l	5.23 (0.88)[b]	5.20 (0.83)[d]	5.06 (0.79)	5.13 (0.82)	$p = 0.001$
SBP not treated, mmHg	117.9 (15.7)	117.7 (13.7)	117.2 (14.4)	117.5 (13.8)	$p = 0.658$
SBP treated, mmHg	125.1 (15.3)	125.4 (15.9)	122.5 (14.2)	127.2 (17.3)	$p = 0.390$
Smoker, n (%)	166 (16.5)	76 (22.6)[d]	98 (13.9)	26 (14.3)	$p = 0.004$
Diabetic, n (%)	39 (3.3)	17 (4.3)	20 (2.6)	1 (0.5)	$p = 0.152$

Values are mean (SD) if not otherwise stated, CVD = cardiovascular disease, HDL = high density lipoprotein, SBP = systolic blood pressure. Only significant ($p < 0.05$) pairwise comparison p values are reported: [a]inactive compared to evening active, [b]inactive compared to moderately active, [c]inactive compared to very active, [d]evening active compared to moderately active, [e]evening active compared to very active, [f]moderately active compared to very active.

* Pairwise comparisons were made if overall p value was significant.

was found in those participants in more active clusters compared to less active clusters.

Competing interests

RA is employed by Polar Electro. The company had no role in the conduct of the study or decision to publish. For the remaining authors none were declared. The results of the study are presented clearly, honestly, and without fabrication, falsification, or inappropriate data manipulation.

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