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Personal Activity Intelligence (PAI), Sedentary Behavior and Cardiovascular Risk Factor Clustering – the HUNT Study

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ABSTRACT

Prolonged sedentary behavior (SB) positively associates with clustering of risk factors for cardiovascular disease (CVD). The recently developed metric for physical activity (PA) tracking called Personal Activity Intelligence (PAI) takes into account age, sex, resting and maximum heart rate, and a score of ≥100 weekly PAI has been shown to reduce the risk of premature CVD death in healthy as well as individuals with known CVD risk factors, regardless of whether or not the current PA recommendations were met. The aim of the present study was to examine if PAI modifies the associations between SB and CVD risk factor (CV-RF) clustering in a large apparently healthy general population cohort (n = 29,950, aged ≥20 years). Logistic regression revealed that in those with ≥100 weekly PAI, the likelihood of CV-RF clustering prevalence associated with prolonged SB was attenuated across age groups. Monitoring weekly PAI-level could be useful to ensure that people perform enough PA to combat SB's deleterious association with CV-RF.

Contents

Statement of Conflict of Interest: see page 93.

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Abbreviations and Acronyms

BP = Blood Pressure

CI = Confidence Interval

CVD = Cardiovascular Disease

CV-RF = Cardiovascular Risk Factor

DM = Diabetes Mellitus

HUNT = The Nord-Trøndelag Health Study

OR = Odds ratio

PA = Physical Activity

PAI = Personal Activity Intelligence

SB = Sedentary Behavior

Sedentary behavior (SB) is defined as behavior in a reclined position (*i.e.* sitting, or lying down), where expenditure of energy does not exceed 1.5 metabolic equivalents of task (METs; 1 MET = 3.5 ml/kg/min).[1] It is estimated that an average adult spends 50–60% of their day in SB.[2]

SB positively associates with risk factors for cardiovascular disease (CVD), and all-cause mortality.[3–7] Previous studies have shown that in those meeting the current physical activity (PA) recommendations, protection from the risk associated with prolonged SB is not guaranteed, identifying SB as a risk factor independent of PA.[8–11] However, a recent study that included over a million individuals showed that the risk of all-cause mortality associated with prolonged SB could be eliminated with high levels (60–75 minutes per day) of moderate intensity PA, while moderate intensity PA congruent with current recommendations was not sufficient in eliminating the risk.[12] However, since only 30% of the population meet the current PA recommendation, asking the remaining 70% of the population who are already not active enough to double the amount of PA outlined by the recommendations may be demotivating and problematic.[13,14]

Recently, a new personalized metric for PA tracking named Personal Activity Intelligence (PAI)[15] was developed with the aim to make it easier to quantify how much PA per week is needed to reduce the risk of premature CVD, the leading cause of death in the world.[15,16] PAI takes into account age, sex, resting and maximum heart rate and is, therefore, a personalized reflection of the body's response to PA.[15] Obtaining ≥100 PAI weekly was found to delay premature death from CVD and all causes, regardless of whether or not the current PA recommendations were met, suggesting that PAI may be an important tool when determining the sufficient amount of PA required to produce significant health benefit in an individual from the general population.[15] However, it is currently unknown if weekly PAI score of ≥100 can counter the negative effects of SB on health, especially in regard to risk of CVD.

Therefore, the primary aim of the current cross-sectional study was to examine the associations of SB and CVD risk factor (CV-RF) clustering, and the potential modifying effect of ≥100 weekly PAI in a large population based cohort of apparently healthy individuals.

Methods

Study population

All inhabitants of Nord-Trøndelag county, aged 20 years and older (n = 100,796), were invited between October 2006 and June 2008 to take part in the third wave of the Nord-Trøndelag Health study (HUNT). Of those, 50,812 (50.4%) accepted the invitation, filled out the invitation letter questionnaire, and underwent clinical examination. All study participants provided informed consent. Detailed account of the HUNT study is described elsewhere.[17] Participants reporting history of heart disease (myocardial infarction, angina pectoris), stroke, prevalent diabetes mellitus (DM) or, regular use of blood pressure (BP) medication and motion impairment were excluded from the current study (n = 15,472). Additionally, we excluded participants with missing values for PAI (n = 852), SB (n = 2818), CV-RF clustering (n = 1254) and smoking status (n = 466). Therefore, 29,950 participants (16,054 women) were included in the current study (Fig 1).

Clinical measurements, questionnaire based information PAI

Trained health personnel measured height, weight and BP. The total sitting time during an average day was based on self-reported data. The question "About how many hours do you sit during an average day?" is similar to the sitting measure of the commonly used International Physical Activity Questionnaire, which has shown acceptable reliability and validity.[18,19] Information on smoking (current, never, former, occasional smoker), civil status, family history of disease, education and leisure time PA was obtained from a self-administered questionnaire; PA questions assessed frequency, intensity and duration of PA. Based on previous studies from our group, intensity of PA as captured by "How hard do you exercise?" question with three response options 1) "no sweat or heavy breathing", 2) "heavy breathing and some sweat" and 3) "push myself to exhaustion", was translated to relative intensity and corresponded to 44%, 73% and 83% of heart rate reserve, respectively.[15] Using this information, weekly PAI was calculated for each participant in the study as recently detailed.[15]

Statistical analyses

Based on the weekly PAI, participants were subdivided into four categories: ≤50 PAI, 51–99 PAI, ≥100 PAI and the inactive group (0 PAI). SB was divided into three sample and sex-specific groups of equal size (tertiles): ≤4 hours per day (h/d), 5–<7 h/d and ≥7 h/d. Descriptive data are presented as mean (standard deviation, SD) for

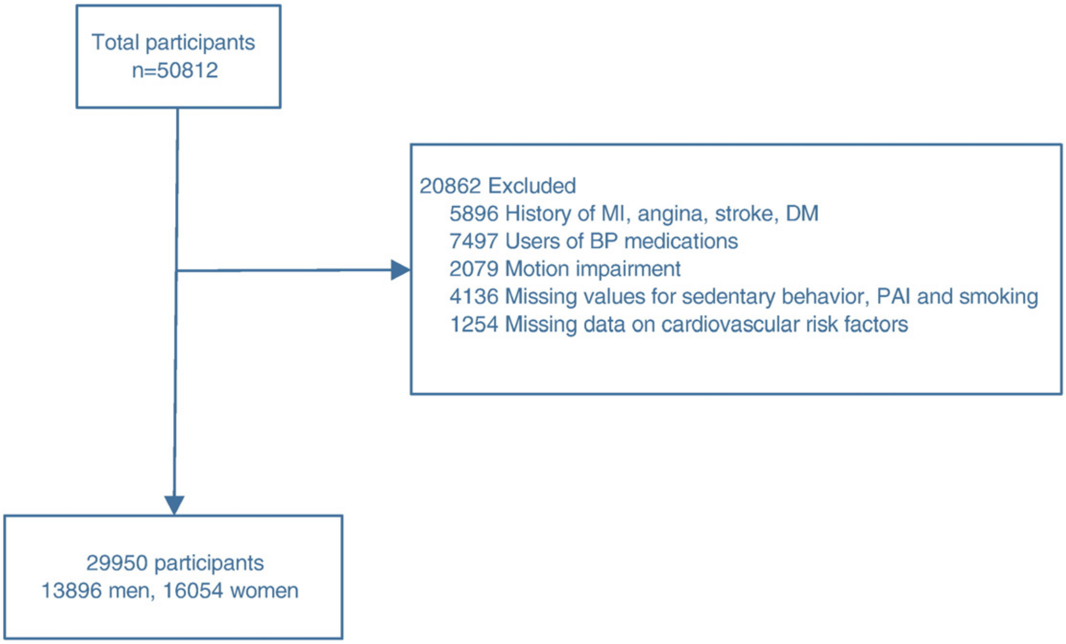

Fig 1 – Flow of participants in the study cohort. ***Abbreviations:*** **MI, myocardial infarction; DM, diabetes mellitus; BP, blood pressure, PAI, personal activity intelligence.**

continuous and as percentages for categorical variables. One-way ANOVA with Bonferroni was used to test differences between continuous, and chi-square was used to test the differences between categorical variables among different PAI categories.

CV-RF was derived from the definition of metabolic syndrome, and the clustering of CV-RF was defined as a waist circumference of ≥94 cm in men and ≥80 cm in women, combined with HDL cholesterol of <1.0 mmol/L in men and <1.3 mmol/L in women, systolic BP ≥130 mm Hg and/or diastolic BP ≥85 mm Hg, and serum triglycerides ≥1.7 mmol/L[20] or medication for hypertension, dyslipidemia or diabetes.

Logistic regression analyses were used to estimate the association of PAI and SB with CV-RF clustering, based on *a priori* decision to stratify by age (≤44, 45–59 and ≥60 years).[19] The basic models were tested for sex interaction ($P > 0.05$), and were therefore adjusted for sex and age, with additional adjustments in further analyses for smoking, non-fasting serum glucose and SB or PAI, respectively. All results are expressed as odds ratios (OR) with the precision of estimates given in 95% confidence intervals (CI).

For the combined associations of PAI and SB with CV-RF clustering, PAI was categorized into two groups (<100 PAI and ≥100 PAI).[15] Participants with ≤4 h/d of SB, and ≥100 weekly PAI were used as a reference. All statistical tests were two sided and a P value of <0.05 was considered statistically significant. The statistical analyses were conducted using IBM SPSS Statistics for Windows, Version 23.0. (IBM Corp. Armonk, NY: IBM Corp.).

Results

The baseline characteristics of the study are presented in Table 1. From the 29,950 apparently healthy participants included, 53.6% were women, 44.1% had ≥100 PAI per week, 17.5% were obese (body mass index ≥30), and 20.7% were found to be inactive. Of the total sample, 5.1% (n = 1541) were categorized as having CV-RF clustering.

SB and CV-RF clustering

Table 2 reports the OR (95% CI) for the prevalence of CV-RF clustering for SB tertiles stratified by age, and adjusted for various confounders. When compared to the reference group (SB ≤4 h/d), those ≤44 years of age reporting SB ≥7 h/d had OR: 1.38 (95% CI, 1.10–1.73) of presenting with CV-RF clustering. Similar was observed for those 45–59 years of age who reported ≥7 h/d of SB, with OR for CV-RF clustering of 1.39 (95% CI, 1.13–1.70) compared to the reference. For participants ≥60 years old, those reporting SB ≥7 h/d had OR of 1.43 (95% CI, 1.10–1.85) for presenting CV-RF clustering compared to the reference group.

PAI and CV-RF clustering

Table 3 reports OR for the prevalence of CV-RF clustering for the four PAI categories, by age and adjusted for various confounders. Among those ≤44 years old, the likelihood for having CV-RF clustering for those inactive (PAI = 0) was 76% higher (OR: 1.76; 95% CI, 1.40–2.20) compared to the reference group with ≥100 PAI. Similarly, having ≤50 PAI was associated with 63% (OR: 1.63; 95% CI, 1.32–2.01), and 47% (OR: 1.47; 95% CI, 1.14–1.89) higher likelihood of having CV-RF clustering compared to the reference in those 45–59, and ≥60 years, respectively. However, having 51–99 PAI was not associated with higher likelihood of CV-RF clustering as compared to having ≥100 PAI across all age categories.

Table 1 – Descriptive characteristics of participants according to Physical Activity Intelligence.

	Personal Activity Intelligence (PAI) [a]			
	0 (n = 6190)	≤50 (n = 7083)	51–99 (n = 3469)	≥100 (n = 13,208)
Women, no. (%)	2418 (39.1)	4183 (59.1)	2140 (61.7)	7313 (55.4)
Age (years)	45.9 (13.5)	51.4 (14.7)	47.4 (14.0)	45.7 (13.6)
Weight (kg)	82.0 (16.0) [c]	77.3 (14.5) [d]	77.8 (15.2) [d]	77.7 (14.0) [d]
Waist circumference (cm)	94.5 (12.3) [c]	92.1 (11.5) [c]	91.4 (11.9) [c]	89.7 (11.0) [c]
Systolic blood pressure (mmHg)	128.0 (16.3) [e]	128.7 (17.8) [e]	126.8 (17.2) [c]	125.6 (15.9) [c]
Diastolic blood pressure (mmHg)	73.5 (11.1) [e]	73.2 (11.1) [e]	72.1 (10.8) [c]	71.5 (10.6) [c]
Total cholesterol (mmol/L)	5.5 (1.1) [f]	5.6 (1.1) [c]	5.5 (1.1) [f]	5.4 (1.1) [c]
HDL cholesterol (mmol/L)	1.3 (0.3) [c]	1.4 (0.4) [g]	1.4 (0.3) [g]	1.4 (0.4) [c]
Glucose (mmol/L)	5.4 (1.3) [e]	5.4 (1.2) [e]	5.3 (1.0) [c]	5.3 (0.9) [c]
Triglycerides (mmol/L)	1.7 (1.1) [c]	1.6 (1.0) [c]	1.5 (0.9) [c]	1.4 (0.9) [c]
BMI (kg/m^2)	27.2 (5.0) [c]	26.6 (4.1) [g]	26.6 (4.2) [g]	26.1 (3.8) [c]
Obesity status, (BMI ≥ 30), no.(%) [h]	1455 (23.5)	1267 (17.9)	644 (18.6)	1875 (14.2)
Smoking, no. (%) [h]				
Never	2328 (37.6)	3062 (43.2)	1616 (46.6)	6691 (50.7)
Former	1542 (24.9)	2095 (29.5)	972 (28.0)	4025 (30.5)
Current	1782 (28.8)	1418 (20.0)	592 (17.1)	1381 (10.5)
Occasional	538 (8.7)	507 (7.2)	289 (8.3)	1111 (8.4)
Sedentary behavior, no. (%) [b,h]				
≤4	2418 (39.1)	2729 (38.5)	1357 (39.1)	4912 (37.2)
5 to <7	1823 (29.5)	2213 (31.2)	1029 (29.7)	3786 (28.7)
≥7	1949 (31.5)	2141 (30.2)	1083 (31.2)	4510 (34.1)

Numbers are mean (SD) unless otherwise stated.
BMI, body mass index.
[a] Sample-specific quartiles of personal activity intelligence (PAI).
[b] In hours per day.
[c] Significantly different from all other PAI categories.
[d] Significantly different from 0 PAI category.
[e] Significantly different from 51–99 PAI and ≥100 PAI category.
[f] Significantly different from ≤50 PAI and ≥100 PAI category.
[g] Significantly different for 0 PAI and ≥100 PAI category.
[h] Significant difference between groups (Chi-square test).

Modifying effect of PAI upon SB and CV-RF clustering

The combined analysis showed that those amounting ≥100 PAI per week were less likely to present with CV-RF clustering associated with SB (Fig 2). In those ≤44 years old, sitting 5–<7 and ≥7 hours per day and having <100 PAI per week resulted in an OR of 1.82 (95% CI, 1.30–2.56) and 2.09 (95% CI, 1.50–2.92), respectively. Similarly, for 45–59 year olds, the OR for those sitting 5–<7 and ≥7 hours per day and having <100 PAI per week were 2.20 (95% CI, 1.61–3.00) and 2.21 (95% CI, 1.61–3 .01), respectively (Fig 2). For the oldest age category (≥60 years), the OR for those sitting 5–<7 and ≥7 hours per day and having <100 PAI per week were 1.93 (95% CI, 1.32–2.84) and 2.29 (95% CI, 1.53–3.44) (Fig 2). However, having ≥100 weekly PAI and sitting for ≥5 hours per day resulted in non-significant ORs across all age categories. For the ≤44, 45–59 and ≥60 year olds in the middle sitting tertile (5–<7 h/d), the ORs were 1.36 (95% CI, 0.93–1.98), 1.25 (95% CI, 0.87–1.78) and 1.30 (95% CI, 0.83–2.03), respectively (Fig 2). Similarly, for the ≤44, 45–59 and ≥60 year olds in the highest sitting tertile (≥7 h/d), the ORs were 1.19 (95% CI, 0.81–1.75), 1.36 (95% CI, 0.96–1.93) and 1.28 (95% CI, 0.77–2.12), respectively (Fig 2).

Table 2 – Adjusted odds ratios (OR) for the prevalence of cardiovascular risk factor (CV-RF) clustering stratified by age according to sedentary behavior (SB) among 29,950 individuals.

Age (years)	≤44			45–59			≥60		
SB (hours/day)	CV-RF Clustering			CV-RF Clustering			CV-RF Clustering		
	Yes	No	OR (95% CI) [a]	Yes	No	OR (95% CI) [a]	Yes	No	OR (95% CI) [a]
≤4	160	4964	1.00 (Reference)	188	3749	1.00 (Reference)	139	2216	1.00 (Reference)
5- < 7	158	3634	1.32 (1.05–1.65)	225	3297	1.34 (1.10–1.64)	171	2170	1.28 (1.01–1.62)
≥7	164	3832	1.38 (1.10–1.73)	223	3284	1.39 (1.13–1.70)	113	1263	1.43 (1.10–1.85)
P-trend			<0.001			<0.001			<0.001

[a] Adjusted for sex, age, smoking status, non-fasting serum glucose and Personal Activity Intelligence (PAI); CI, confidence interval.

Table 3 – Adjusted odds ratios (OR) for the prevalence of cardiovascular risk factor (CV-RF) clustering stratified by age according to personal activity intelligence (PAI) category among 29,950 individuals.

Age (years)	≤44			45–59			≥60		
PAI	CV-RF Clustering			CV-RF Clustering			CV-RF Clustering		
	Yes	No	OR (95%CI) [a]	Yes	No	OR (95%CI) [a]	Yes	No	OR (95%CI) [a]
0	175	2795	1.76 (1.40–2.20)	186	2015	1.93 (1.56–2.40)	101	918	2.06 (1.54–2.75)
≤50	86	2234	1.28 (0.98–1.68)	180	2420	1.63 (1.32–2.01)	164	1999	1.47 (1.14–1.89)
51–99	53	1466	1.25 (0.91–1.72)	68	1175	1.29 (0.97–1.71)	47	660	1.23 (0.86–1.77)
≥100	168	5935	1.00 (Reference)	202	4720	1.00 (Reference)	111	2072	1.00 (Reference)
P-trend			<0.001			<0.001			<0.001

CI, confidence interval.
[a] Adjusted for sex, age, smoking status, non-fasting serum glucose and sedentary behavior SB.

Discussion

The main finding of the current study is that having a score of ≥100 PAI per week attenuates the negative association between prolonged SB and CV-RF clustering in apparently healthy participants from the general population.

We observed a positive association between SB and CV-RF clustering. In a previous study on the same cohort this relation between CV-RF clustering and SB was found to persist regardless of whether or not the PA recommendations were met, suggesting SB is a risk factor for CVD independent of PA.[11] This is also consistent with findings from other studies on the general population.[4,7,21] In a meta-analysis which included more than 700,000 participants from 16 prospective and 2 cross-sectional studies, prolonged SB was associated with a 147% increase in the risk of CVD, 112% increase in the risk of DM, 90% increase in risk of CVD mortality and 49% increase in the risk of all-cause mortality, with the reported associations largely independent of PA.[4] Yet, a more recent meta-analysis, which included 16 studies and over 1 million individuals, showed that high levels of moderate intensity PA (420–525 minutes per week) eliminated the risk of premature all-cause and CVD death associated with prolonged SB.[12] However, it may be problematic to prescribe 420 to 525 weekly minutes of moderate intensity PA to individuals already deemed inactive (below the current PA recommendation).

The current study demonstrated that obtaining ≥100 PAI per week attenuated the association between CV-RF clustering and prolonged SB across age groups. A weekly PAI score of 100 can be accumulated using PA of various amounts and intensities. For instance, amounting 150 minutes of moderate intensity PA (~44% heart rate reserve), corresponding to meeting the PA recommendation, earns approximately 38 PAI. However, the higher the intensity of PA, the higher the PAI score. The goal of 100 PAI can be achieved by amounting a minimum of 40 weekly minutes (35 weekly minutes less than recommendation) in vigorous intensity PA (~85% heart rate reserve). Obtaining a score of 100 PAI, therefore, may be more achievable as it is individualized and allows for any personal preference of intensity and duration.

Furthermore, a score of 51–99 PAI per week in our study was associated with lower prevalence of CV-RF clustering across age groups, suggesting a dose–response relationship between PAI and CV-RF clustering. Thus, even a PAI score lower than 100 may be beneficial for health. In fact, it has been shown that major health benefits occur between least active and less active individuals so any activity in highly sedentary persons will go a long way.[15] However, in a study on the general population, no further risk reductions in premature death or loss of benefit were seen with a score beyond a 100 PAI.[15]

The strength of the current study is its large sample size across all age categories, representing the general Norwegian population free from heart disease, with detailed information on various CV-RF. The study had some limitations. SB was self-reported and thus susceptible to recall bias. Although, the questionnaire on SB utilized in the current study is similar to the commonly used International Physical Activity Questionnaire, which has been validated and found acceptably reliable[18] objective measures of SB would have been preferable. Furthermore, PAI algorithm was derived from the HUNT cohort and as such, its generalizability remains to be tested in other populations with varying ethnicities, age, health and disease status.

In conclusion, our results show that a score of ≥100 weekly PAI attenuates the association between SB and CV-RF clustering across adult age categories in a general Norwegian population. Monitoring weekly PAI-level could be useful to ensure that people spending long time in a sedentary state perform enough PA to reduce the risk of CVD. Certainly, increasing PA and reducing SB is needed throughout the globe as a cost-effective approach to improve overall health and, especially, reduce CVD-and all-cause mortality.[22–25]

Statement of conflict of interest

Professor Wisløff is the inventor of PAI, and share holder (together with, the major share holdershareholder NTNU Technology Transfer Office, and three other enterprises; Femto incInc., Singsaker holding and Berre Holding inc.Inc.) of a company (Beatstack incInc.) that holds the IP rights for PAI. Physical Enterprises inc.Inc. that develops an application that may utilize data from diverse heart rate monitors, as well as developing wearable's that incorporates PAI owns

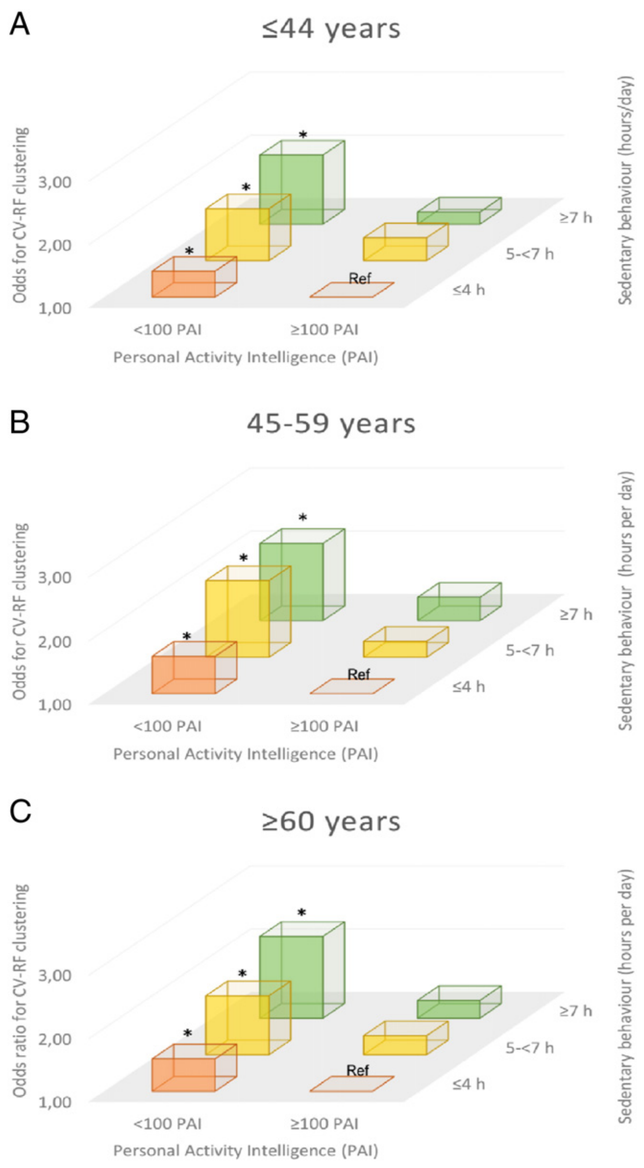

Fig 2 – Adjusted odds ratios[a] of clustering of CV-RF in combined categories of PAI and SB. [a]Adjusted for sex, age, smoking status, and non-fasting serum glucose. * denotes significant difference ($P < 0.05$) from reference category.

Beatstack inc.Inc. Due to the potential conflict of interest, we are thankful to the Head of Science at Department of Circulation and Medical Imaging, professor Ola Dale, who monitored adherence to design, and statistical analysis in the current study. There are no further disclosures or potential conflicts of interest to report.

Acknowledgments

The study was funded by grants from the K.G. Jebsen Foundation, the Norwegian Research Council, the Liaison Committee between the Central Norway Regional Health Authority and the Norwegian University of Science and Technology. The funding organizations had no role in the design and execution of the study, in the collection, analysis, and interpretation of the data or in the preparation, review, or approval of the manuscript. We have read and understood the policy of the Progress in Cardiovascular Diseases and declare the following: Professor Wisløff is the inventor of PAI, and share holder (together with, the major share holder-shareholder NTNU Technology Transfer Office, and three other enterprises; Femto incInc., Singsaker holding and Berre Holding inc.Inc.) of a company (Beatstack incInc.) that holds the IP rights for PAI. Physical Enterprises inc.Inc. that develops an application that may utilize data from diverse heart rate monitors, as well as developing wearable's that incorporates PAI owns Beatstack inc.Inc. Due to the potential conflict of interest, we are thankful to the Head of Science at Department of Circulation and Medical Imaging, professor Ola Dale, who monitored adherence to design, and statistical analysis in the current study. There are no further disclosures or potential conflicts of interest to report. The Nord-Trøndelag Health Study (HUNT) is a collaboration between the HUNT Research Center (Faculty of Medicine, Norwegian University of Science and Technology), the Nord-Trøndelag County Council and the Norwegian Institute of Public Health. We are grateful to the HUNT study participants and management for using these data. The funding organizations had no role in the design and execution of the study, in the collection, analyses, and interpretation of the data, or in the preparation, review, or approval of the submitted manuscript.

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