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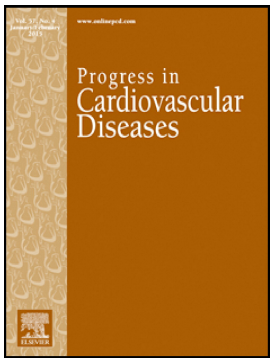

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Temporal Changes in a Novel Metric of Physical Activity Tracking (Personal Activity Intelligence) and Mortality: the HUNT Study, Norway

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Conflict of interest: Professor Wisløff is the inventor of PAI, and shareholder (together with, the major shareholder NTNU Technology Transfer Office, and three other enterprises; Femto inc, Singsaker holding and Berre Holding inc.) of a company (Beatstack inc) that holds the IP rights for PAI. Physical Enterprises 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. 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.

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Abstract:

Background: Personal Activity Intelligence (PAI) is a novel activity metric that translates heart rate variations during exercise into a weekly score. Weekly PAI scores assessed at a single point in time were found to associate with lower risk of premature cardiovascular disease (CVD) mortality in the general healthy population. However, to date, the associations between long-term longitudinal changes in weekly PAI scores and mortality have not been explored.

Purpose: The aim of the present study was to prospectively examine the association between change in weekly PAI scores estimated 10 years apart, and risk of mortality from CVD and all-causes.

Methods: We performed a prospective cohort study of 11,870 men and 13,010 women without known CVD in Norway. By using data from the Nord-Trøndelag Health Study (HUNT) PAI was estimated twice, ten years apart (HUNT1 1984-86 and HUNT2 1995-97). Mortality was followed-up until December 31, 2015. Adjusted hazard ratios (AHR) and 95% confidence intervals (CI) for death from CVD and all-causes related to temporal changes in PAI were estimated using Cox regression analyses.

Results: During a mean (SD) of 18 (4) years of follow-up, there were 4782 deaths, including 1560 deaths caused by CVD. Multi-adjusted analyses demonstrated that participants achieving a score of ≥100 PAI at both time points had 32% lower risk of CVD mortality (AHR 0.68; CI: 0.54-0.86) for CVD mortality and 20% lower risk of all-cause mortality (AHR 0.80; CI: 71-0.91) compared with participants obtaining <100 weekly PAI at both measurements. For participants having <100 PAI in HUNT1 but ≥100 PAI in HUNT2, the AHRs were 0.87 (CI: 0.74-1.03) for CVD mortality, and 0.86 (CI: 0.79-0.95) for all-cause mortality. We also found an inverse linear relationship between change in PAI and risk of CVD mortality among participants with 0 PAI (P<0.01), and ≤50 PAI (P=0.04) in HUNT1,

indicating that an increase in PAI over time is associated with lower risk of mortality. Excluding the first three years of follow-up did not substantially alter the findings. Increasing PAI score from <100 PAI in HUNT1 to ≥100 PAI in HUNT2 was associated with 6.6 years gained lifespan.

Conclusion: Among men and women without known CVD, an increase in PAI score and sustained high PAI score over a 10-year period was associated with lower risk of mortality.

Abbreviations:

BMI Body Mass Index

BP Blood pressure

CRF Cardiorespiratory fitness

CVD Cardiovascular disease

DM Diabetes Mellitus

HDL High Density Lipoprotein

HTN Hypertension

HUNT The Nord-Trøndelag health study

NCD Non-communicable disease

PA Physical activity

PAI Personal Activity Intelligence

TG Triglyceride

Introduction

Non-communicable diseases (NCDs) are the leading cause of mortality worldwide and account for 70% of all deaths every year (1, 2). Cardiovascular disease (CVD) is the most common type of NCD, and is estimated to be responsible for approximately 17.5 million deaths globally (3, 4). There is strong epidemiological evidence demonstrating an inverse relationship between physical activity (PA) levels and risk of mortality for CVD and all-causes (5-8). Prospective studies have shown that increasing PA levels over time reduces the risk of CVD and all-cause mortality (6). There is evidence showing that for the same amount of PA volume, high intensity PA is associated with greater mortality risk reductions compared to moderate or low intensity PA (7, 8). This may be because high intensity PA is superior to improve cardiorespiratory fitness (CRF) (9-12), which is inversely associated with CVD risk profile and mortality risk in the general population (13-16). Despite this, most of the PA goals used in health promotion (10,000 steps per day, 30 minutes of PA per day) do not take exercise intensity into consideration. Further, only approximately 30% of the Norwegian population and 5% of the American population meet the current PA recommendations (5, 17, 18). Hence, innovative approaches to promote individual participation in PA are needed (19).

A major challenge in PA promotion is to provide different options, and individual feedback tailored to personal needs and preferences (20). Most available PA metrics in the literature fail to translate physiological measures into meaningful, personal and scientifically proven information for the mainstream user (21). Recently, we developed a personalized activity metric, named Personal Activity Intelligence (PAI) (22). PAI considers the individual's sex, age, resting and maximal heart rates, and reflects individuals' response to PA (22). The metric translates heart rate variations over the course of a week, into a simple and easily understandable score (0=inactive, and 100=active enough) (22). For instance, a score of 100 PAI can be obtained by performing various PA volumes and intensities, as long as the

heart rate is elevated above a certain threshold (22). As the PAI metric favors high intensity PA, a score of 100 PAI approximates 40 weekly minutes of high intensity PA (≈85% of heart rate reserve), or 60 weekly minutes of PA at an intensity of ≈75% of heart rate reserve (22).

Achieving a score of ≥100 PAI weekly was found to attenuate the association between sedentary behavior and CVD risk factor clustering (23). Further, achieving 100 PAI was associated with lower risk of mortality from CVD and all-causes in the general healthy population, as well as in patients with CVD, independent of meeting PA guidelines (22, 24). This suggests that PAI may be a useful tool when quantifying the PA needed to produce substantial health benefit in individuals from the general population (22). However, previous studies on PAI rely on a single baseline assessment. Potential confounders may bias studies addressing single exposure assessment, and PA levels reported at baseline may change during follow-up, affecting the risk estimates. Temporal changes in PAI scores and risk of CVD and all-cause mortality have not been previously considered. Therefore, the association between sustaining a low/adequate PAI score, or increasing/decreasing PAI score over time, and mortality is unknown. The aim of this study was to prospectively examine the association between changes in weekly PAI scores estimated 10 years apart, and risk of mortality from CVD and all-causes.

Methods

Study population

We included participants aged 20 years and older from the Nord-Trøndelag County who participated both in the first (HUNT1, January 1984 to February 1986) and the second (HUNT2, August 1995 to June 1997) survey of the Nord-Trøndelag health study. All participants provided informed consents, filled out detailed questionnaires about health and life style, and attended clinical examinations at both HUNT surveys. Detailed accounts of the first and second HUNT surveys have been previously described (25). Of the 77 212 subjects who participated in HUNT1, 47 313 (61%) also participated in HUNT2 (25). We excluded 5006 subjects with self-reported CVD, 3 537 subjects with somatic disease (moderate or high), 1 677 subjects with motion impairment (moderate or high) and 12 213 subjects with missing values on covariates (Figure 1) (22). The remaining 24 880 participants were included in the study. The Regional Ethical Committee for Health research approved the study protocol (2017/318/REKmidt).

Clinical Measurements and Questionnaire Based Information

Trained nurses performed clinical measurements such as height, weight, blood pressure (BP), and laboratory measurements, such as non-fasting serum concentrations of glucose, triglycerides (TGs), total cholesterol and high-density lipoprotein (HDL) cholesterol. Measurement methods are described elsewhere (26). Body mass index (BMI) was categorized into four groups according to the World Health Organization's BMI classification (27). Hypertension (HTN) was defined as measured systolic BP ≥140 mmHg or diastolic BP≥90 mmHg or self-reported use of anti-HTN drugs. Diabetes mellitus (DM) status was determined based on self-reported diagnosis or non-fasting glucose levels >11.1 mmol/l (28). High total cholesterol was defined as >6.9 mmol/l for participants under 50 years and >7.8 mmol/l for

participants above 50 years (29). Low levels of HDL-cholesterol were defined as <1.2 mmol/l for women and <1.0 mmol/l for men whereas high levels of TGs were defined as >1.7 mmol/l (30).

Participants with self-reported CVD (myocardial infarction or angina pectoris or stroke/brain hemorrhage) were identified using the first HUNT1 and HUNT2 questionnaire (31, 32). Information about DM, use of anti-HTN drugs, somatic disease, motion impairment, smoking status, alcohol consumption, educational level, and age was also obtained from the first HUNT2 questionnaire (32).

Personal Activity Intelligence (PAI)

Information on leisure time PA was obtained from a self-administered questionnaire. PAI scores for each participant, were calculated using the responses to PA questions about duration, frequency and intensity in both HUNT1 and HUNT2 (32, 33). The reported intensity of PA was translated to relative intensity where low, moderate or vigorous intensity corresponded to 44%, 73% and 83% of heart rate reserve, respectively. According to the PAI algorithm described elsewhere (22, 23), the weekly minutes spent performing PA were obtained by multiplying the average frequency of PA with the average duration of PA. We then combined the exercise volumes with the reported exercise intensities by the use of heart rate reserves to estimate a weekly PAI score.

Outcomes

The primary outcome was mortality caused by CVD (International Classification of Diseases, ninth revision: 390-459 or International Classification of Diseases, tenth revision: I00-I99), and the secondary outcome was mortality from all causes. Data on cause and date of death was obtained from the Norwegian cause of death registry, and accurately matched to each

participant through their 11-digit personal identification number. Our study had a virtually complete follow-up of participants, as registration in the population registers is mandatory in Norway. Only participants who emigrated from the country are missing in the analyses (≤1%). The participants were followed from their participation date in HUNT2 until their date of death or end of follow-up on 31st December 2015.

Statistical analyses

To compare baseline characteristics, categorical data was assessed using Chi-square test or Fisher's exact test according to the estimated expected values. Continuous data was compared using one-way ANOVA with equal or unequal variances.

To assess the association between change in the weekly PAI score and the risk of mortality from CVD and all-causes, the participants' PAI score achieved in both HUNT1 and HUNT2 (collected ten years apart) were divided into two groups: ≥100 PAI and <100 PAI. This, resulted in four different categories of change in PAI: <100 PAI at both HUNT1 and HUNT2, ≥ 100PAI at HUNT1 and < 100PAI at HUNT2; <100 PAI at HUNT1 and ≥100 PAI at HUNT2; ≥100 PAI at both HUNT1 and HUNT2. This cut-off point was chosen a priori based on results from previous studies (22, 23). The rate of death per 1 000 person-years was estimated in each PAI change group. The four PAI change groups were then compared using a Cox regression analysis separately for CVD mortality and all-cause mortality. The first model was adjusted for age and sex. The second model was further adjusted for education (<10 years; 10-12 years; >12 years), alcohol consumption over two weeks (abstainer; <8 drinks; 8-14 drinks; >14 drinks), smoking status (yes or no), DM status (yes or no), hypertension status (yes or no), BMI (<18.5; 18.5-24.9; 25-29.9; ≥30 kg/m^2), total cholesterol (normal or high), HDL-cholesterol (low or normal), and TGs (normal or high). In both models, attained age was included as the time scale. To test the proportional hazards

assumption, Schoenfeld residuals were used and time interactions were added to the variables. When the assumption was not met, stratified results are reported. Further, we estimated years of life gained as the difference in 10^{th} percentile survival years associated with the four different change groups using Laplace regression (34, 35). The analysis was sex adjusted. Sub-groups analyses were performed for participants 65 years or older.

To assess the association between continuous change in PAI and risk of mortality from CVD and all-causes, we estimated the difference between obtained PAI in HUNT1 and HUNT2, and categorized the differences into groups of 30 PAI to allow for the assessment of the trend. As previous physical fitness has been associated with risk of mortality (36), we assessed linear trends in different sub-groups of obtained PAI in HUNT1 (0 PAI; 1-50 PAI; 51-99 PAI; ≥100 PAI), using the multi-adjusted model previously described. Sensitivity analyses were performed by excluding the first three years of follow-up.

Descriptive data are presented as means (standard deviations) and frequencies (percentages). Survival data are reported as hazard ratios with 95% confidence intervals. All the analyses were performed using Stata version 14.2. All statistical tests were two-sided and considered significant at *P*-value lower than 0.05.

RESULTS

Baseline characteristics of participants are presented in Table 1 and Table 2. At both time points (HUNT 1 and/or HUNT 2), participants with a PAI score ≥100 were younger, more educated and appeared to be healthier (lower BMI, lower percentage of HTN and DM, and more favorable blood biochemistry profiles) compared to participants with a PAI score <100 (Table 1). Similar results are observed when comparing participants according to their temporal change in PAI levels (Table 2).

During the median follow-up of 19.3 years (interquartile range 18.8-19.9; 447 405 person-years), there were 4 782 deaths, including 1 560 deaths caused by CVD. Compared to participants who sustained low PAI scores (<100 PAI at both HUNT1 and HUNT2), multi-adjusted analyses demonstrated that participants who sustained high PAI scores (≥100 PAI at both HUNT1 and HUNT2) had 32% lower risk of CVD mortality (95% CI: 14% to 46%), and 20% lower risk of all-cause mortality (95% CI: 9% to 29%) (Table 3). For participants who increased their PAI scores over time (PAI score of <100 at HUNT1 and ≥100 at HUNT2), the adjusted hazard ratio was 0.87 (95% CI: 0.74 to 1.03) for CVD mortality, and 0.86 (95% CI: 0.79 to 0.95) for all-cause mortality.

In the analyses using PAI as continuous variable, we found an inverse linear relationship between change in PAI and risk of mortality among participants with PAI score of 0 (P=0.003 for all-cause mortality, and P=0.006 for CVD mortality), and PAI score of ≤50 (P<0.001 for all-cause mortality, and P=0.04 for CVD mortality) at HUNT1, indicating that an increase in PAI over time is associated with decreased risk of mortality (Table 4). Among participants with >50 PAI at HUNT1, we found no evidence of trend associated with change in PAI and risk of mortality. Sensitivity analyses demonstrated that results were not substantially altered by excluding the first three years of follow-up (supplementary material Table 1 and Table 2).

We observed that, adjusted for sex, participants with ≥100 PAI at both HUNT1 and HUNT2 had 8.2 (95% CI: 7.4 to 9.0) years of life gained compared to those with <100 PAI at both assessments (Figure 2). For those who increased their PAI score over time (<100 PAI at HUNT1, ≥100 PAI at HUNT2), the corresponding years gained were 6.6 (95% CI: 5.7 to 7.4), whereas participants who were active in HUNT1 (≥100 PAI) but decreased their score had 2.9 (95% CI: 2.05 to 3.8) years of life gained. For participants who were 65 years or older at HUNT2, ≥100 PAI at both assessments was associated with 3.4 (95% CI: 2.3 to 4.5) years of life gained, compared to <100 PAI at both HUNT1 and HUNT2 (data not shown).

DISCUSSION

In this prospective study of apparently healthy men and women, we found that an increase in PAI over a 10-year period was associated with lower risk of mortality, and that participants with a weekly PAI score of ≥100 at both time points had the lowest risk of CVD and all-cause mortality.

PAI levels estimated in HUNT1 were previously found to associate with lower risk of mortality among individuals from the general population as well as in patients with CVD (22, 24), and healthy men and women obtaining ≥100 PAI had respectively 23% and 17% lower risk of CVD mortality, and 13% and 17% lower risk of all-cause mortality (22). In this current study, we found that obtaining ≥100 PAI at two different points in time is associated with 32% lower risk of CVD mortality and 20% lower risk of all-cause mortality. Noteworthy, the previous study assessing PAI and risk of mortality was only supported by a single PAI calculation. However, levels of PA may change over time resulting in a misclassification of PA levels. This may bias the results and underestimate the estimated risk reductions (37). In this current study, temporal changes in PAI were accounted for, and we found larger risk reductions in regard to CVD and all-cause mortality compared to results using a single PAI calculation. Therefore, our findings strengthen the knowledge about PAI and health outcomes by showing that 100 PAI is strongly related to health and longevity. This may further encourage development of PAI and promote adherence to PA using a contemporary and innovative approach.

When studying continuous changes of physical activity, we found a relationship between increasing PAI levels over time and risk of mortality from CVD and all-causes, only among individuals obtaining ≤50 weekly PAI at HUNT1. PAI takes into account both intensity and time spent performing PA, and the PAI score is proportional to intensity of PA: when performing PA of the same duration, high intensity earns a higher PAI score compared

to moderate or low intensity (22). Therefore, PAI is founded on mechanistic interactions between PA and CRF. Interestingly, high levels of CRF in the past, despite low current CRF level, has been associated with lower risk of mortality (36). This may explain our current findings of association between PAI and risk of mortality only among individuals obtaining ≤50 PAI at the first measurement. In practical terms, this suggests that encouraging individuals to improve their PAI score is most essential among inactive individuals obtaining ≤50 PAI at first assessment.

The main strength of the current study was that it was the first study to assess a novel metric of PA tracking (PAI) at two different points in time (10 years apart), enabling study of behavioral changes in PA in an innovative way. Further, the study has a relatively large sample size, a long-term and virtually complete follow up, and a comprehensive source of information on possible confounding factors. The study also has some limitations. Data used to exclude participants and to estimate PAI was self-reported and therefore prone to information bias, however the questionnaires adopted to collect PA data have shown acceptable reliability and validity (38, 39). Despite the large number of study participants, the number of events in certain sub-groups was low (e.g. only one event among the subgroup of individuals obtaining 51-99 PAI in HUNT1 who increased their PAI score by 15 to 45 PAI at HUNT2 (Table 4)) which affects the precision of the corresponding effect estimates. Therefore, one should be careful in drawing firm conclusions related to these subgroups. Moreover, participants included in the current study and in previous studies assessing PAI were predominantly Caucasians (22), therefore research on the risk of mortality associated with PAI in different races and ethnicities is warranted. Finally, even though participants at risk were excluded from the study and results were adjusted for possible known confounders, unknown underlying factors may still confound our estimates.

The PAI algorithm has recently been integrated into a wearable device and a downloadable application (compatible with most Bluetooth enabled heart rate monitors). The application analyzes heart rate variations continuously over the course of a week to calculate an individual score, providing instant user feedback on the amount of PAIs earned. Physicians are able to follow their patients' PAI score over time as PAI score may be shared between patients and physicians. Our findings may therefore encourage physicians to recommend their patients to reach 100 PAI and increase their PAI score over time. This may further translate into improved health benefits in the general inactive population.

Conclusion: In this prospective study of apparently healthy men and women, an increase in PAI and sustained high PAI score of ≥100 PAI obtained ten years apart was associated with lower risk of mortality from CVD and all-causes.

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Figure legends

Figure 1. Flow of participants

CVD, cardiovascular disease; HUNT, Helseundersøkelse i Nord-Trøndelag (Nord-Trøndelag Health Study); HDL: High density lipoprotein

Figure 2. Survival curves by PAI score, adjusted for sex

PAI, Personal Activity Intelligence; H, Helseundersøkelse i Nord-Trøndelag (Nord-Trøndelag Health Study)

Table 1 Baseline characteristics of study participants by PAI score in HUNT-1 and HUNT-2 (n=24 880)

	PAI score in HUNT 1					PAI score in HUNT 2				
	<100 (n=19 386)		≥100 (n=5 494)		*P*-value	<100 (n=17 643)		≥100 (n=7 237)		*P*-value
Age, years, mean (SD)	52.7	(12.8)	50.1	(11.7)	<0.001	53.4	(13.0)	48.9	(11.0)	<0.001
BMI, kg/m^2, mean (SD)										
≤ 18.5	92	(0.5)	14	(0.3)		82	(0.5)	24	(0.3)	
18.6 - 24.9	7 351	(37.9)	2 294	(41.8)	<0.001	6 409	(36.3)	3 236	(44.7)	<0.001
25.0-29.9	8 760	(45.2)	2 519	(45.9)		8 069	(45.7)	3 210	(44.4)	
≥ 30.0	3 183	(16.4)	667	(12.1)		3 083	(17.5)	767	(10.6)	
Hypertension status, N (%)[1]										
Yes	9 063	(46.8)	2 304	(41.9)	<0.001	8 611	(48.8)	2 756	(38.1)	<0.001
No	10 323	(53.3)	3 190	(58.1)		9 032	(51.2)	4 481	(61.9)	
Smoking, N (%)										
Yes	5 747	(29.7)	1 092	(19.9)	<0.001	5 192	(29.4)	1 647	(22.8)	<0.001
No	13 639	(70.4)	4 402	(80.1)		12 451	(70.6)	5 590	(77.2)	
Alcohol consumption, N (%)[2]										
Abstainer	2 438	(12.6)	390	(7.1)		2 273	(12.9)	555	(7.7)	
0 - 7 glasses	14 719	(75.9)	4 183	(76.1)	<0.001	13 360	(75.7)	5 542	(76.6)	<0.001
8 - 14 glasses	1 804	(9.3)	741	(13.5)		1 643	(9.3)	902	(12.5)	
>14 glasses	425	(2.2)	180	(3.3)		367	(2.1)	238	(3.3)	
Education, N (%)										
< 10 y	7 937	(40.9)	1 436	(26.1)		7 538	(42.7)	1 835	(25.4)	
10-12 y	8 185	(42.2)	2 461	(44.8)	<0.001	7 288	(41.3)	3 358	(46.4)	<0.001
> 12 y	3 264	(16.8)	1 597	(29.1)		2 817	(16.0)	2 044	(28.2)	
Diabetes, N (%)										
Yes	512	(2.6)	90	(1.6)	<0.001	478	(2.7)	124	(1.7)	<0.001
No	18 874	(97.4)	5 404	(98.4)		17 165	(97.3)	7 113	(98.3)	
Total cholesterol, N (%)										
Normal	17 144	(88.4)	4 965	(90.4)	<0.001	15 524	(88.0)	6 585	(91.0)	
High	2 242	(11.6)	529	(9.6)		2 119	(12.0)	652	(9.0)	
HDL cholesterol, N (%)										
Low	5 335	(27.5)	1 215	(22.1)	<0.001	4 974	(28.2)	1 576	(21.8)	<0.001
Normal	14 051	(72.5)	4 279	(77.9)		12 669	(71.8)	5 661	(78.2)	
Triglycerides, N (%)										
Normal	11 534	(59.5)	3 520	(64.1)	<0.001	10 198	(57.8)	4 856	(67.1)	<0.001
High	7 852	(40.5)	1 974	(35.9)		7 445	(42.2)	2 381	(32.9)	
Physical activity, N (%)										
Light intensity										
None	1 489	(8.0)	149	(3.2)		1 571	(9.0)	67	(1.2)	
<1 hour	3 688	(19.9)	517	(11.1)	<0.001	3 976	(22.8)	229	(4.0)	<0.001
1-2 hours	7 419	(40.0)	1 799	(38.6)		7 567	(43.4)	1 651	(28.8)	
≥3 hours	5 933	(32.0)	2 197	(47.1)		4 335	(24.8)	3 795	(66.1)	
Vigorous intensity										
None	6 574	(45.6)	853	(18.5)		7 427	(63.0)	-		
<1 hour	4 134	(28.7)	1 089	(23.6)	<0.001	4 365	(37.0)	858	(11.9)	<0.001
1-2 hours	2 665	(18.5)	1 604	(34.7)		-		4 269	(59.0)	
≥3 hours	1 033	(7.2)	1 077	(23.3)		-		2 110	(29.2)	

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in square meters), HDL, High Density Lipoprotein.
[1]Defined as measured systolic blood pressure ≥ 140, diastolic blood pressure ≥ 90 or self-reported use of antihypertensive drugs.
[2]Based on consumption the last 14 days.

Table 2 Characteristics of study participants according to temporal change in PAI score from HUNT1to HUNT2

	HUNT-2 <100				HUNT-2 ≥100				
	HUNT-1 <100 (n=15 008)		HUNT-1 ≥100 (n=2 635)		HUNT-1 <100 (n=4 378)		HUNT-1 ≥100 (n=2 859)		*P*-value
Age, years, mean (SD)	53.8	(13.0)	51.3	(12.5)	48.9	(11.2)	49.0	(10.8)	<0.001
BMI, kg/m^2, mean (SD)									
≤ 18.5	75	(0.5)	7	(0.3)	17	(0.4)	7	(0.2)	
18.6 - 24.9	5 445	(36.3)	964	(36.6)	1 906	(43.5)	1 330	(46.5)	<0.001
25.0-29.9	6 822	(45.5)	1 247	(47.3)	1 938	(44.3)	1 272	(44.5)	
≥ 30.0	2 666	(17.8)	417	(15.8)	517	(11.8)	250	(8.7)	
Hypertension status, N (%)[1]									
Yes	7 387	(49.2)	1 224	(46.5)	1 676	(38.3)	1 080	(37.8)	<0.001
No	7 621	(50.8)	1 411	(53.6)	2 702	(61.7)	1 779	(62.2)	
Smoking, N (%)									
Yes	4 562	(30.4)	630	(23.9)	1 185	(27.1)	462	(16.2)	<0.001
No	10 446	(69.6)	2 005	(76.1)	3 193	(72.9)	2 397	(83.8)	
Alcohol consumption, N (%)[2]									
Abstainer	2 075	(13.8)	198	(7.5)	363	(8.3)	192	(6.7)	
0 - 7 glasses	11 320	(75.4)	2 040	(77.4)	3 399	(77.6)	2 143	(75.0)	<0.001
8 - 14 glasses	1 311	(8.7)	332	(12.6)	493	(11.3)	409	(14.3)	
>14 glasses	302	(2.0)	65	(2.5)	123	(2.8)	115	(4.0)	
Education, N (%)									
< 10 y	6 699	(44.6)	839	(31.8)	1 238	(28.3)	597	(20.9)	
10-12 y	6 098	(40.6)	1 190	(45.2)	2 087	(47.7)	1 271	(44.5)	<0.001
> 12 y	2	(14.7)	606	(23.0)	1 053	(24.1)	991	(34.7)	

	211								
Diabetes, N (%)									
Yes	424	(2.8)	54	(2.1)	88	(2.0)	36	(1.3)	<0.001
No	14 584	(97.2)	2 581	(98.0)	4 290	(98.0)	2 823	(98.7)	
Total cholesterol, N (%)									
Normal	13 185	(87.9)	2 339	(88.8)	3 959	(90.4)	2 626	(91.9)	<0.001
High	1 823	(12.2)	296	(11.2)	419	(9.6)	233	(8.2)	
HDL cholesterol, N (%)									
Low	4 270	(28.5)	704	(26.7)	1 065	(24.3)	511	(17.9)	<0.001
Normal	10 738	(71.6)	1 931	(73.3)	3 313	(75.7)	2 348	(82.1)	
Triglycerides, N (%)									
Normal	8 671	(57.8)	1 527	(58.0)	2 863	(65.4)	1 993	(69.7)	<0.001
High	6 337	(42.2)	1 108	(42.0)	1 515	(34.6)	866	(30.3)	
Physical activity, N (%)									
Light intensity									
None	1 443	(9.7)	128	(5.0)	46	(1.3)	21	(1.0)	
<1 hour	3 528	(23.7)	448	(17.4)	160	(4.4)	69	(3.3)	<0.001
1-2 hours	6 419	(43.1)	1 148	(44.7)	1 000	(27.4)	651	(31.1)	
≥3 hours	3 488	(23.4)	847	(32.9)	2 445	(67.0)	1 350	(64.6)	
Vigorous intensity									
None	6 574	(65.6)	853	(48.4)	-		-		
<1 hour	3 454	(34.4)	911	(51.6)	680	(15.5)	178	(6.2)	<0.001
1-2 hours	-		-		2 665	(60.9)	1 604	(56.1)	
≥3 hours	-		-		1 033	(23.6)	1 077	(37.7)	

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in square meters), HDL,
High Density Lipoprotein. [1] Defined as measured systolic blood pressure ≥ 140, diastolic blood pressure ≥ 90 or self-reported use of antihypertensive drugs. [2] Based on consumption the last 14 days.

Table 3 Hazard ratios of death from CVD and all-causes by PAI (Personal Activity Intelligence) score in HUNT 1 (H1) and HUNT 2 (H2)

PAI	Deaths	Person-years	Rate[1]	HR (95% CI)[2]	HR (95% CI)[4]
CVD death					
Continually low PAI	1 163	264 897	4.4	1.00 (Reference)[3]	1.00 (Reference)[5]
Decreased PAI	142	47 513	3.0	0.83 (0.69-0.99)	0.87 (0.73-1.04)
Increased PAI	172	81 532	2.1	0.81 (0.69-0.96)	0.87 (0.74-1.03)
Continually high PAI	83	53 463	1.6	0.56 (0.45-0.70)	0.68 (0.54-0.86)
				P-trend <0.001	*P-trend = 0.001*
All-cause death					
Continually low PAI	3 453	264 897	13.0	1.00 (Reference)	1.00 (Reference)[6]
Decreased PAI	457	47 513	9.6	0.87 (0.79-0.96)	0.92 (0.83-1.01)
Increased PAI	549	81 532	6.7	0.81 (0.74-0.89)	0.86 (0.79-0.95)
Continually high PAI	323	53 463	6.0	0.69 (0.61-0.77)	0.80 (0.71-0.91)
				P-trend <0.001	*P-trend <0.001*

CVD: Cardiovascular Disease; HR: Hazard ratio; CI: Confidence intervals.
Continually low PAI: <100 in HUNT1, <100 in HUNT2, decreased PAI: ≥100 in HUNT1, <100 in HUNT2, increased PAI: <100 in HUNT1, ≥100 in HUNT2, continually high PAI: ≥100 in HUNT1, ≥100 in HUNT2.

[1]Calculated per 1000 person-years

[2]HR adjusted for age (age adjusted time scale) and sex

[3]Stratified by sex

[4]HR adjusted for age (age-adjusted time scale), sex, education (<10, 10-12, >12 y), alcohol (abstainer; <8; 8-14; >14 glasses per fortnight), smoking status (yes/no), diabetes (yes/no), hypertension (yes/no), BMI (<18.5; 18.5-24.9; 25-29.9; ≥30 kg/m^2), total cholesterol (normal/high), HDL cholesterol (low/normal), triglycerides (normal/high)

[5]Stratified by sex, total cholesterol, hypertension and BMI

[6]Stratified by smoking status, BMI, total cholesterol and alcohol

Table 4 Deaths from all-cause and CVD by changes in Personal Activity Intelligence (PAI) from HUNT 1 to HUNT 2

	HUNT 1 [=0]		**HUNT 1 [≤50]**		**HUNT 1 [51-99]**		**HUNT 1 [≥100]**	
PAI change	All-cause[1]	CVD[2]	All-cause[1]	CVD[2]	All-cause[1]	CVD[2]	All-cause[1]	CVD[2]
>75	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)	1.00 (reference)
45 to 75	0.91 (0.76 - 1.10)	0.87 (0.61 - 1.25)	1.05 (0.84 - 1.32)	1.14 (0.76 - 1.70)	1.07 (0.60 - 1.91)	0.91 (0.31 - 2.65)	1.05 (0.71 - 1.55)	0.67 (0.25 - 1.85)
15 to 45	1.01 (0.88 - 1.15)	1.10 (0.86 - 1.40)	1.23 (1.05 - 1.44)	1.27 (0.96 - 1.68)	1.65 (0.94 - 2.90)	0.65 (0.08 - 4.98)	0.89 (0.49 - 1.60)	1.60 (0.57 - 4.55)
-15 to 15	1.20 (1.05 - 1.37)	1.34 (1.05 - 1.71)	1.21 (1.04 - 1.40)	1.23 (0.94 - 1.60)	1.39 (1.03 - 1.89)	1.16 (0.62 - 2.18)	1.04 (0.73 - 1.49)	1.39 (0.66 - 2.96)
-15 to -45	-	-	1.52 (1.25 - 1.86)	1.49 (1.05 - 2.13)	1.04 (0.74 - 1.45)	0.98 (0.50 - 1.90)	0.97 (0.71 - 1.32)	1.62 (0.87 - 3.01)
-45 to -75	-	-	1.45 (0.84 - 2.52)	1.38 (0.53 - 3.58)	1.12 (0.84 - 1.49)	1.11 (0.63 - 1.96)	1.32 (0.96 - 1.81)	1.87 (0.98 - 3.55)
<-75	-	-	-	-	1.58 (1.04 - 2.39)	2.20 (1.00 - 4.82)	1.06 (0.83 - 1.34)	1.41 (0.84 - 2.35)
P-trend	*0.003*	*0.006*	*<0.001*	*0.048*	*0.243*	*0.256*	*0.518*	*0.108*

CVD: cardiovascular disease, PAI change: PAI changes from HUNT1 to HUNT2 categorized in intervals of 30 PAI

Hazard ratios adjusted for age (age-adjusted time scale), education (<10y, 10-12 y, >12 y), alcohol (<8; 8-14; >14 glasses per fortnight), smoking status (yes/no), diabetes (yes/no), hypertension (yes/no), BMI (<18.5; 18.5-24.9; 25-29.9; ≥30 kg/m^2), total cholesterol (normal/high), HDL cholesterol (low/normal), and triglycerides (normal/high).

[1]Stratified by smoking status, BMI, total cholesterol.

[2]Stratified by smoking status, BMI, total cholesterol, sex and hypertension status.

Conflict of interest: Professor Wisløff is the inventor of PAI, and shareholder (together with, the major shareholder NTNU Technology Transfer Office, and three other enterprises; Femto inc, Singsaker holding and Berre Holding inc.) of a company (Beatstack inc) that holds the IP rights for PAI. Physical Enterprises 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. 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.

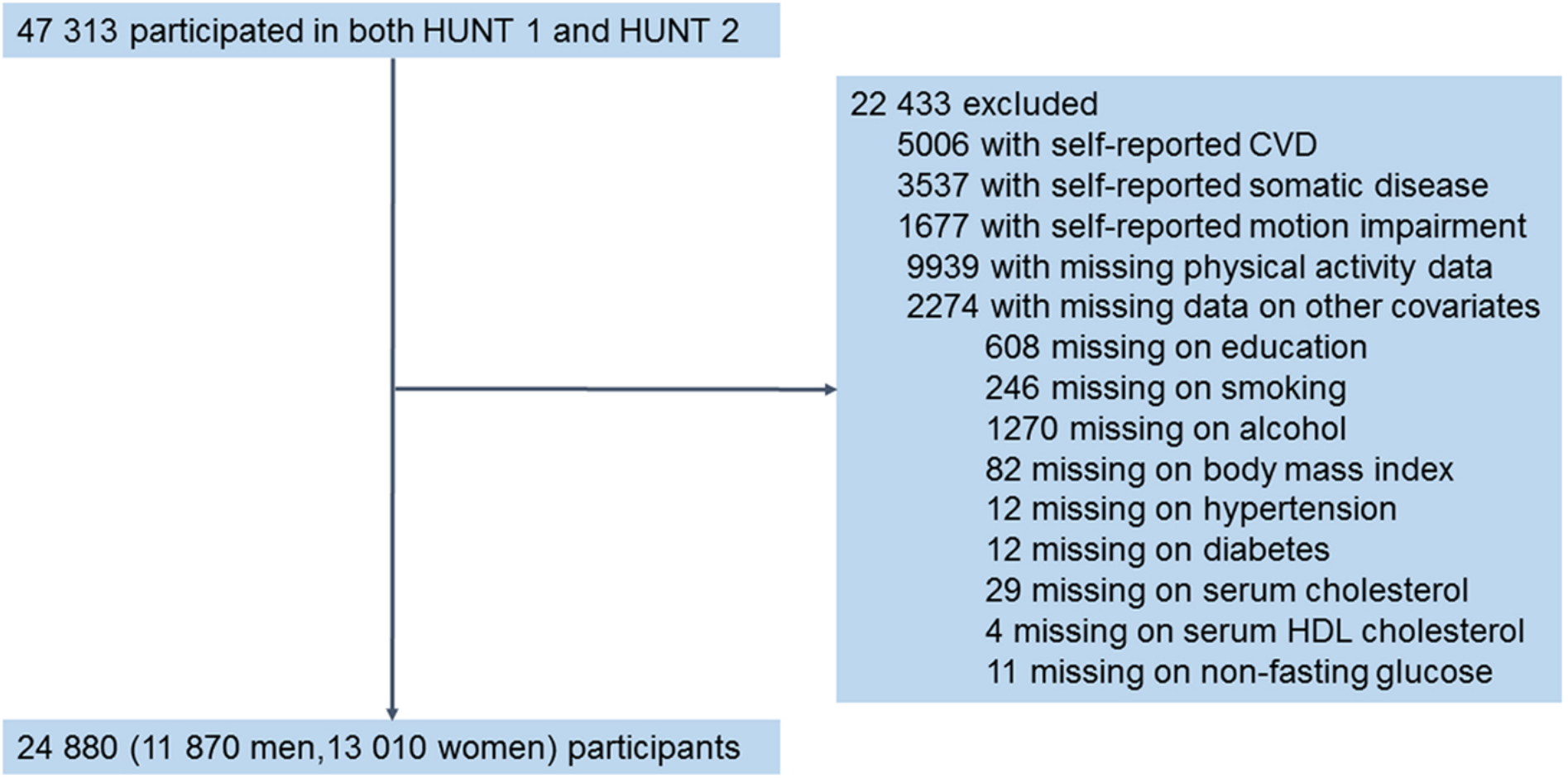
47 313 participated in both HUNT 1 and HUNT 2
22 433 excluded
5006 with self-reported CVD
3537 with self-reported somatic disease
1677 with self-reported motion impairment
9939 with missing physical activity data
2274 with missing data on other covariates
608 missing on education
246 missing on smoking
1270 missing on alcohol
82 missing on body mass index
12 missing on hypertension
12 missing on diabetes
29 missing on serum cholesterol
4 missing on serum HDL cholesterol
11 missing on non-fasting glucose
24 880 (11 870 men,13 010 women) participants

Figure 1

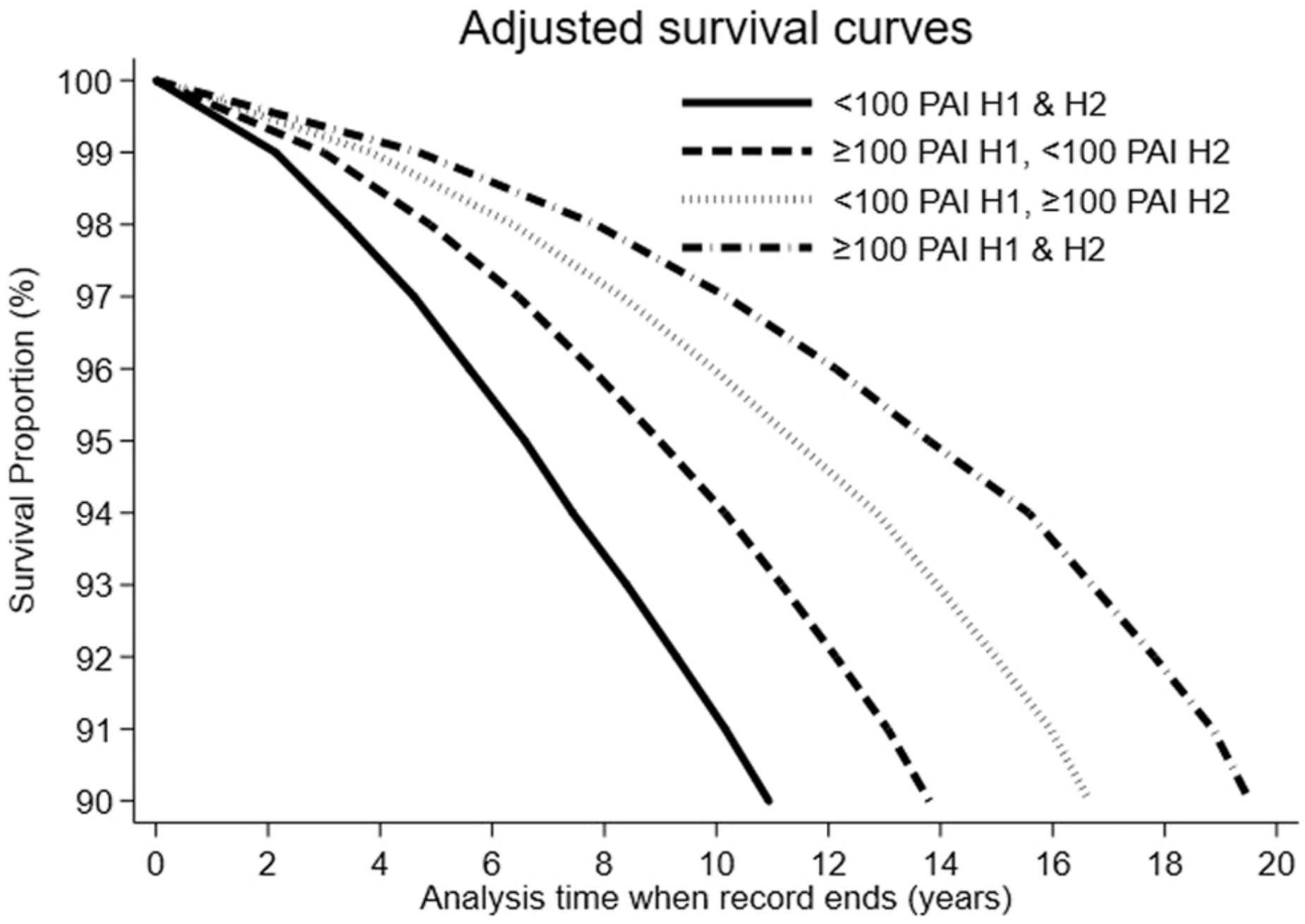
Adjusted survival curves
<100 PAI H1 & H2
≥100 PAI H1, <100 PAI H2
<100 PAI H1, ≥100 PAI H2
≥100 PAI H1 & H2
Survival Proportion (%)
100
99
98
97
96
95
94
93
92
91
90
0
2
4
6
8
10
12
14
16
18
20
Analysis time when record ends (years)

Figure 2