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ORIGINAL ARTICLE

Personal Activity Intelligence and Mortality in Patients with Cardiovascular Disease: The HUNT Study

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Abstract

Objective: To test whether Personal Activity Intelligence (PAI), a personalized metric of physical activity (PA) tracking, is associated with all-cause and cardiovascular disease (CVD) mortality in patients with self-reported CVD and to determine whether these associations change depending on whether contemporary PA recommendations are met.

Patients and Methods: A total of 3133 patients with CVD (mean [SD] age, 67.6 [10.3] years; 64% men) were followed from the date of participation in the Nord-Trøndelag Health Study (between January 1, 1984, and February 28, 1986) until the date of death or the end of follow-up (December 31, 2015). The participants' weekly PAI score was calculated and divided into 4 groups (PAI scores of 0, ≤50, 51-99, and ≥100). We used Cox proportional hazards regression models to estimate hazard ratios for CVD and all-cause mortality rates.

Results: After mean follow-up of 12.5 years (39,157 person-years), there were 2936 deaths (94%), including 1936 CVD deaths. Participants with weekly PAI scores of 100 or greater had 36% (95% CI, 21%-48%) and 24% (95% CI, 10%-35%) lower risk of mortality from CVD and all causes, respectively, compared with the inactive group. Participants had similar risk reductions associated with their weekly PAI scores regardless of following contemporary PA recommendations or not.

Conclusion: Obtaining a weekly PAI score of at least 100 was associated with lower mortality risk from CVD and all causes in individuals with CVD regardless of whether the current PA recommendations were met.

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Cardiovascular disease (CVD) is the leading cause of death globally and accounts for approximately 17.5 million deaths every year.[1,2] Physical activity (PA) is a cornerstone in the secondary prevention of CVD and is associated with a lower risk of mortality from CVD and all causes.[3-5] Consequently, individuals are encouraged to perform at least 150 minutes of moderate-intensity PA or 75 minutes of high-intensity PA or a combination of both weekly.[6] Furthermore, there are also suggestions that high-intensity exercise may be superior in improving the heart in health and disease.[7,8]

Unfortunately, although studies support the efficacy of PA recommendations regarding lowering the risk of CVD and all-cause mortality,[3,9] 83% of patients with CVD fail to meet the current PA recommendations.[10-12] Earlier reports have shown significant benefits at PA levels much below the recommended quantity,[3,5,13,14] which challenge the precision of the contemporary PA recommendations. Recently, we developed Personal Activity Intelligence (PAI),[15] a personalized PA metric that considers the individual's sex, age, and resting and maximum heart rate and reflects the body's response to PA by translating heart rate variations, by the mean of heart rate reserves, over a week into a simple and easily understandable score. Obtaining a weekly PAI score of at least 100 was found to be associated with a lower risk of CVD and all-cause mortality in the general population without CVD and to attenuate the association between sedentary behavior and CVD risk factor clustering in healthy individuals,

For editorial comment, see page 1158

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regardless of whether the current PA recommendations were met.[15,16] This suggests that PAI may be a useful tool when quantifying the PA needed to produce a substantial health benefit in individuals from the general population.[15]

A PAI score of 100 can be obtained by performing PA of various amounts and intensities. The PAI score is proportional to the intensity of PA: when performing PA of the same duration, high intensity earns a higher PAI score compared with moderate intensity. For example, meeting the current PA recommendations by accumulating a minimum of 150 minutes at moderate intensity (~44% of the heart rate reserve) earns a PAI score of approximately 38. In comparison, 40 minutes of high-intensity PA (~85% of the heart rate reserve) results in a PAI score of approximately 100.[15] Regarding selection of intensity and duration of PA, PAI is tailored to the individual and allows for personal preferences. Therefore, one can choose the activity and intensity of preference as long as 100 PAI is accumulated over 7 days.

The beneficial effects of high-intensity exercise in patients with CVD has been widely reported[7,8,14,17-19]; however, it remains unclear whether a weekly PAI score is associated with risk of mortality in individuals already diagnosed as having CVD.

Therefore, the aim of this study was to examine the association between weekly obtained PAI score and risk of mortality from CVD and all causes in participants with CVD and in subgroups of hypertensive and overweight patients with CVD. Furthermore, we sought to determine whether the association between obtained PAI score and risk of mortality was similar regardless of whether the current PA recommendations were met.

METHODS

Study Population

From January 1, 1984, through February 28, 1986, the entire eligible adult population (n=86,404) aged 20 years or older from Nord-Trøndelag county in Norway were invited to participate in the first wave of the Nord-Trøndelag Health Study (HUNT1). Of those invited, 77,201 (89%) accepted the invitation. All the participants provided informed consent. They underwent a clinical examination and completed detailed questionnaires on health and lifestyle.[20,21] A detailed account of the HUNT study is described elsewhere.[22] In total, 5458 participants self-reported to have CVD, defined as angina pectoris or myocardial infarction (MI) or stroke. We excluded 1438 participants with missing values on PA; 886 with missing values on smoking status, educational level, alcohol consumption, body mass index (BMI), hypertension, motion impairment, or somatic disease; and 1 who died on the date of inclusion (Figure 1). The remaining 3133 participants constituted the study sample. The study protocol was approved by the Regional Committee for Medical and Health Research Ethics in Central Norway.

Clinical and Questionnaire-Based Information

The first HUNT1 questionnaire[20] was used to identify individuals with CVD, motion impairment, and somatic disease. Cardiovascular disease was defined as self-reported MI, angina pectoris, stroke, or cerebral hemorrhage. Motion impairment and somatic disease resulting in long-term functional impairment and limitations in PA participation were also self-reported and were categorized into 2 groups: absent (none or mild) and present (moderate or severe). Furthermore, the same questionnaire was used to assess the participants' sex, age, self-reported health, and use of blood pressure–lowering medication. The second HUNT1 questionnaire[21] was used to assess each participant's alcohol consumption, educational level, smoking status, and diabetes status. Smoking status was categorized into 2 groups: yes (current smoker) and no (never or previous smoker). Trained nurses assessed clinical information such as height, weight, resting heart rate, and blood pressure. Measurement methods have been previously described.[22] The BMI was calculated as the weight in kilograms divided by the height in meters squared. Participants were classified into 4 BMI categories: less than 18.5, 18.5 to 24.9, 25.0 to 29.9, and 30.0 or greater according to the World Health Organization classification.[23]

PAI and PA Recommendations

The PAI score was obtained at baseline for each participant using the following questions from the second HUNT1 questionnaire[21]: 1) How often do you exercise (on average) (never, less than once a week, 2-3 times a week, or nearly

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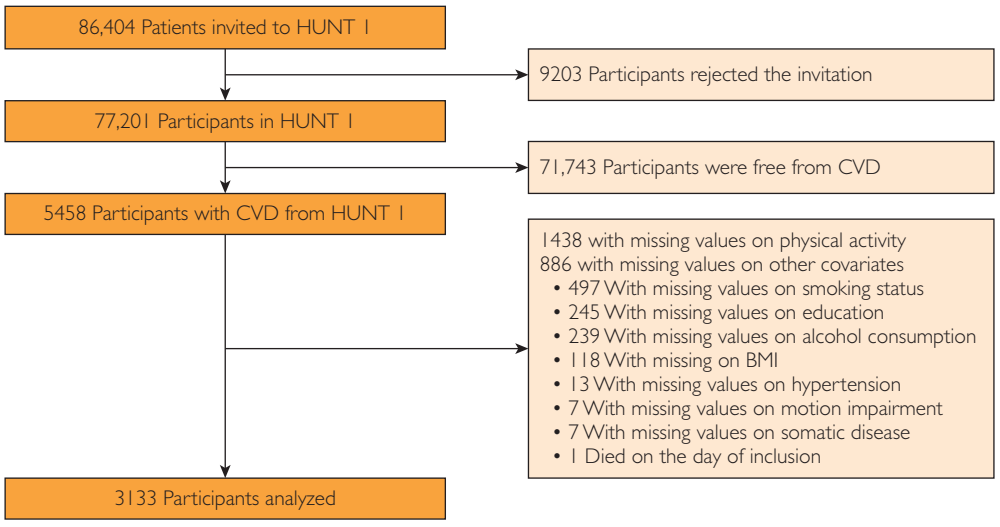

FIGURE 1. Flow of participants. BMI = body mass index; CVD = cardiovascular disease; HUNT = Helseundersøkelse i Nord-Trøndelag (Nord-Trøndelag Health Study).

every day)? 2) If you exercise as often as once or several times a week, how hard do you exercise (on average) (I take it easy, I don't get out of breath or break a sweat, I push myself until I'm out of breath and break into a sweat, or I practically exhaust myself)? 3) For how long do you exercise each time (on average) (<15 minutes, 16-30 minutes, 30 minutes to 1 hour, or >1 hour)? Participants who responded "never" or "less than once a week" to the frequency question were coded as zero. Total exercise time in minutes per week was calculated by multiplying the average duration of exercise with the average frequency of exercise sessions. For example, reporting "between 30 and 60 minutes" and "2 -3 times a week" was interpreted as 45 min × 2.5 = 112.5 min/wk. The 3 intensity options correspond to 44%, 73%, and 83% of heart rate reserve.[15] According to the PAI algorithm previously described elsewhere,[15,16] we combined the exercise volumes with the reported exercise intensities by the use of heart rate reserves to estimate a weekly PAI score. Similarly, we combined frequency and duration of PA with the reported intensities to estimate whether participants were following contemporary PA recommendations.[6]

Outcomes

The primary outcome of the study was CVD mortality (*International Classification of Diseases, Ninth Revision* codes 390-459; *International Classification of Diseases, Tenth Revision* codes I00-I99), and the secondary outcome was all-cause mortality. Participants were followed from the date of participation in HUNT1 until the date of death or the end of follow-up (December 31, 2015), whichever came first. Data on cause and time of death were obtained from the National Cause of Death Registry and were linked to each participant through their personal identification number, permitting accurate matching. Norwegian physicians and public health officers are directed to report all deaths to the National Cause of Death Registry in Norway, thus this study had virtually complete follow-up.

Statistical Analyses

Baseline characteristics were compared using the χ^2 test for categorical data. The Fisher's exact test was used for groups with expected numbers less than 5. A 1-way analysis of variance with equal or unequal variances was used to compare continuous data. To investigate the association between PAI score and risk of mortality, we categorized participants into 4 groups according to their level of PAI achieved over 1 week: 0 (inactive), 50 or less, 51 to 99, or 100 or more. The inactive group (0 PAI) was used as a reference. The rate of death per 100 person-years of observation was

TABLE 1. Baseline Characteristics of the 3133 Study Participants[a]

Characteristic	Personal Activity Intelligence score				*P* value
	0 (n=1280)	≤50 (n=1432)	51-99 (n=199)	≥100 (n=222)	
Women (No. [%])	566 (44.2)	450 (31.4)	82 (41.2)	25 (11.3)	<.001
Age (y), mean (SD)	68.7 (11.0)	67.4 (9.2)	67.5 (8.6)	62.1 (12.1)	<.001
BMI, kg/m^2 (No. [%])					
<18.5	23 (1.8)	10 (0.7)	1 (0.5)	1 (0.5)	
18.5-24.9	441 (34.5)	500 (34.9)	80 (40.2)	85 (38.3)	.001
25.0-29.9	570 (44.5)	701 (49.0)	97 (48.7)	111 (50.0)	
≥30.0	246 (19.2)	221 (15.4)	21 (10.6)	25 (11.3)	
Hypertension status (No. [%])[b]					
Yes	952 (74.4)	1020 (71.2)	132 (66.3)	141 (63.5)	
Medication	89 (7.0)	110 (7.7)	19 (9.6)	13 (5.9)	.002
No	239 (18.7)	302 (21.1)	48 (24.1)	68 (30.6)	
Smoking (No. [%])					
Yes	373 (29.1)	358 (25.0)	39 (19.6)	49 (22.1)	.004
No	907 (70.9)	1074 (75.0)	160 (80.4)	173 (77.9)	
Alcohol consumption (No. [%])[c]					
Abstainer	295 (23.1)	259 (18.1)	49 (24.6)	28 (12.6)	
None	724 (56.6)	781 (54.5)	100 (50.3)	99 (44.6)	
1-4 times	186 (14.5)	307 (21.4)	40 (20.1)	68 (30.6)	<.001
5-10 times	20 (1.6)	26 (1.8)	3 (1.5)	13 (5.9)	
>10 times	55 (4.3)	59 (4.1)	7 (3.5)	14 (6.3)	
Somatic disease (No. [%])					
Yes	420 (32.8)	405 (28.3)	52 (26.1)	62 (27.9)	.03
No	860 (67.2)	1027 (71.7)	147 (73.9)	160 (72.1)	
Motion impairment (No. [%])					
Yes	274 (21.4)	210 (14.7)	29 (14.6)	23 (10.4)	<.001
No	1006 (78.6)	1222 (85.3)	170 (85.4)	199 (89.6)	
Education (No. [%])					
<10 y	1138 (88.9)	1196 (83.5)	171 (85.9)	154 (69.4)	
10-12 y	102 (8.0)	157 (11.0)	20 (10.1)	39 (17.6)	<.001
>12 y	40 (3.1)	79 (5.5)	8 (4.0)	29 (13.1)	
Physical activity (No. [%])					
Frequency					
Inactive[d]	1280 (100)	-	-	-	
Once a week	-	470 (32.8)	25 (12.6)	13 (5.9)	
2-3 times a week	-	545 (38.1)	-	123 (55.4)	<.001
Almost every day	-	417 (29.1)	174 (87.4)	86 (38.7)	
Duration per session (min)					
<30	-	922 (64.4)	12 (6.0)	47 (21.2)	<.001
≥30	-	510 (35.6)	187 (94.0)	175 (78.8)	
Intensity per session					
Easy	-	1395 (97.4)	164 (82.4)	-	
Out of breath	-	37 (2.6)	33 (16.6)	213 (96.0)	<.001
Near exhaustion	-	-	2 (1.0)	9 (4.1)	

[a]BMI = body mass index. Dashes represent no data/no participants.
[b]Hypertension was defined as follows: yes (measured systolic blood pressure ≥140 mm Hg or diastolic blood pressure ≥90 mm Hg); no, or medication (measured systolic blood pressure <140 mm Hg and diastolic blood pressure <90 mm Hg and self-reported use of antihypertensive drugs).
[c]Based on consumption in the past 14 days.
[d]Defined as never or less than once a week.

calculated in each group. The different groups were then compared, separately for CVD deaths and all-cause deaths, using a Cox regression analysis adjusted for several covariates. The first model included sex and attained age using an age-adjusted time scale. The second, multiple-adjusted, model further included somatic disease (present [moderate or severe] or absent), motion impairment (present [moderate or severe] or absent), smoking status (yes or no),

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TABLE 2. HRs for Death From CVD and All Causes by PAI Score[a]

Type of death and PAI score	Deaths (No.)	Person-years of observation	Rate[b]	HR (95% CI)[c]	HR (95% CI)[d]
CVD death					
0 (Inactive)	796	14,395	5.5	1.00 (Reference)	1.00 (Reference)[e]
≤50	901	18,497	4.9	0.83 (0.75-0.91)	0.84 (0.76-0.93)
51-99	126	2708	4.7	0.80 (0.67-0.97)	0.84 (0.69-1.03)
≥100	113	3557	3.2	0.61 (0.50-0.74)	0.64 (0.52-0.79)
P for trend				<.001	<.001
All-cause death					
0 (Inactive)	1202	14,395	8.4	1.00 (Reference)	1.00 (Reference)[f]
≤50	1354	18,497	7.3	0.83 (0.76-0.89)	0.86 (0.80-0.94)
51-99	190	2708	7.0	0.80 (0.69-0.94)	0.86 (0.74-1.01)
≥100	190	3557	5.3	0.69 (0.59-0.80)	0.76 (0.65-0.90)
P trend trend				<.001	<.001

[a]CVD = cardiovascular disease; HR = hazard ratio; PAI = Personal Activity Intelligence.
[b]Calculated per 100 person-years of observation.
[c]Adjusted for age and sex (age-adjusted time scale), stratified by sex.
[d]Adjusted for age, sex, body mass index, hypertension, smoking status, alcohol consumption, educational level, motion impairment, and somatic impairment.
[e]Stratified by sex, somatic disease, alcohol consumption, and educational level.
[f]Stratified by sex, somatic disease, and motion impairment.

hypertension (yes [measured systolic blood pressure ≥140 mm Hg or measured diastolic blood pressure ≥90 mm Hg], no, or on medication but below criteria), alcohol consumption (abstainer, none, 1-4 times, 5-10 times, or >10 times), level of education (<10, 10-12, or >12 years), and BMI (<18.5, 18.5-24.9, 25.0-29.9, and ≥30.0). Results are reported as hazard ratios with 95% CIs. The assumption of proportional hazards was tested using Schoenfeld residuals and by the addition of time interactions with the covariates. When the proportional hazards assumption was not met, stratified results are reported. We then performed sensitivity analyses by excluding the first 3 years of follow-up. Similarly, subgroup analyses were performed to assess hazard rates in participants with higher mortality risk. In a separate sex-adjusted analysis, we used Laplace regression to calculate the years of life lost as a difference in median survival years associated with obtaining PAI scores less than100 and 100 or greater.[24,25] Subgroup analyses were performed on participants 70 years and younger and older than 70 years of age.

Furthermore, we categorized the participants into those with PAI scores less than 100 and 100 or greater and into meeting and not meeting the PA recommendations from the World Health Organization.[6] The following category was used as reference: PAI score of 100 or greater and meeting the recommendations. Combined associations of PAI score and PA recommendations were assessed across 4 groups while controlling for various confounders. All the statistical tests were performed using Stata Statistical Software: Release 14 (StataCorp LP). The tests were 2-sided and considered significant at $P<.05$.

RESULTS

We included 3133 participants (64% men; mean [SD] age, 67.6 [10.3] years). Of these participants, 1228 (39%) had experienced an MI, 2074 (66%) had angina pectoris, and 648 (21%) had experienced a stroke or cerebrovascular disease. During mean follow-up of 12.5 years (39,157 person-years), there were 2936 deaths (94%), including 1936 CVD deaths (62%).

The baseline characteristics of the participants are presented in Table 1. Participants with high PAI levels were younger and more educated. An increasing PAI score was associated with a lower percentage of participants with hypertension, smoking, somatic disease, and motion impairment.

A high PAI score was associated with lower risk of CVD and all-cause mortality ($P<.001$). Multiple-adjusted analyses demonstrated that

TABLE 3. HRs for Death According to PA Recommendations and PAI Score[a]

Type of death and PAI score	PA recommendations	Participants (No.)	Deaths (No.)	Person-years of observation	Rate[b]	HR (95% CI)[c]	HR (95% CI)[d]
CVD deaths							
≥100	Yes	101	51	1575	3.24	1.00 (Reference)	1.00 (Reference)[e]
	No	121	62	1982	3.13	1.14 (0.79-1.66)	1.14 (0.78-1.67)
<100	Yes	0	-	-	-	-	-
	No	2911	1823	35,599	5.12	1.58 (1.19-2.09)	1.49 (1.12-1.99)
All-cause deaths							
≥100	Yes	101	87	1575	5.52	1.00 (Reference)	1.00 (Reference)[f]
	No	121	103	1982	5.20	1.14 (0.85-1.51)	1.18 (0.89-1.57)
<100	Yes	0	-	-	-	-	-
	No	2911	2746	35,599	7.71	1.39 (1.12-1.72)	1.30 (1.05-1.61)

[a]HR = hazard ratio; PA = physical activity; PAI = Personal Activity Intelligence. Dashes represent no data/no participants.
[b]Calculated per 100 person-years of observation.
[c]Adjusted for age and sex (age-adjusted time scale), stratified by sex.
[d]Adjusted for age, sex, body mass index, hypertension, smoking status, alcohol consumption, educational level, motion impairment, and somatic impairment.
[e]Stratified by sex, somatic disease, alcohol, and educational level.
[f]Stratified by sex and somatic disease.

compared with inactive participants, those obtaining a weekly PAI score of at least 100 had 36% (95% CI, 21%-48%) and 24% (95% CI, 10%-35%) lower risk of CVD and all-cause mortality, respectively (Table 2). There were no further risk reductions or loss of benefit observed beyond obtaining a weekly PAI score of 100 or greater. Excluding the first 3 years of follow-up did not alter the results (data not shown).

Participants obtaining a weekly PAI score of at least 100 had similar risk reductions regardless of whether they were following today's advice for PA (Table 3). Compared with participants obtaining at least 100 PAI and meeting the official PA recommendations, those who did not meet the PA recommendations but had a PAI score of at least 100, the hazard ratios were 1.14 (95% CI, 0.78-1.67) and 1.18 (95% CI, 0.89-1.57) for CVD and all-cause mortality, respectively.

Adjusted subgroup analyses are presented in Tables 4 (CVD mortality) and 5 (all-cause mortality). Obtaining a score of 100 PAI or greater was associated with similar mortality risk reductions for both sexes and different age groups. Compared with the inactive group, a weekly PAI score of 100 or greater resulted in 53% (95% CI, 6%-77%) and 36% (95% CI, 20%-48%) CVD mortality risk reductions for women and men, respectively (Table 4). Compared with the reference group, reductions in risk of CVD mortality were observed for those younger and older than 70 years with a score of at least 100 PAI (41% [95% CI, 25%-55%] and 44% [95% CI, 21%-60%], respectively) (Table 4). The associations were comparable for all-cause mortality (Table 5). Furthermore, compared with the inactive reference group, obtaining 100 PAI or greater was associated with 40% (95% CI, 24%-53%), 28% (95% CI, 5%-45%), and 41% (95% CI, 22%-56%) lower mortality risk from CVD among participants with CVD with hypertension, overweight (BMI, 25.0-29.9), and those with poor self-reported health, respectively (Table 4). We observed comparable risk reductions for all-cause mortality (Table 5). No significant risk reductions of having a weekly PAI score of 100 or greater were observed in patients with CVD who were smokers or had diabetes (Tables 4 and 5).

We observed that, adjusted for sex, a PAI score less than 100 was associated with 4.7 years (95% CI, 3.2-6.3 years) of life lost compared with a PAI score of at least 100 (Figure 2). For those 70 years and younger and those older than 70 years, the corresponding years of life lost were 4.3 (95% CI, 1.6-7.0) and 3.3 (95% CI, 1.7-4.8), respectively (data not shown).

DISCUSSION

The finding that a weekly PAI score of 100 or greater was associated with reduced risk of

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TABLE 4. HRs for Death From CVD in Subgroups, by Personal Activity Intelligence Score[a,b]

Subgroup	Personal Activity Intelligence score				*P* value[c]
	0 (n=1280)	≤50 (n=1432)	51-99 (n=199)	≥100 (n=222)	
Men					
Deaths (No.)	442	626	82	105	
HR (95% CI)	1.00 (Reference)	0.88 (0.78-0.99)	0.91 (0.72-1.15)	0.64 (0.52-0.80)	
Women					
Deaths (No.)	354	275	44	8	
HR (95% CI)	1.00 (Reference)	0.75 (0.64-0.88)	0.66 (0.48-0.91)	0.47 (0.23-0.94)	.21
Age ≤70 y					
Deaths (No.)	368	513	75	73	
HR (95% CI)	1.00[d] (Reference)	1.00 (0.88-1.15)	1.07 (0.84-1.37)	0.59 (0.45-0.75)	
Age >70 y					
Deaths (No.)	428	388	51	40	
HR (95% CI)	1.00 (Reference)	0.72 (0.63-0.83)	0.56 (0.42-0.76)	0.56 (0.40-0.79)	.09
Hypertension: yes					
Deaths (No.)	624	661	81	78	
HR (95% CI)	1.00[d] (Reference)	0.78 (0.70-0.88)	0.72 (0.57-0.90)	0.60 (0.47-0.76)	
Hypertension: medication					
Deaths (No.)	59	67	13	5	
HR (95% CI)	1.00 (Reference)	0.82 (0.57-1.17)	0.68 (0.37-1.25)	0.38 (0.15-0.96)	.11
Hypertension: no					
Deaths (No.)	113	173	32	30	
HR (95% CI)	1.00 (Reference)	1.06 (0.84-1.35)	1.33 (0.90-1.98)	0.78 (0.52-1.17)	
BMI: 18.5-24.9					
Deaths (No.)	269	312	50	40	
HR (95% CI)	1.00[d] (Reference)	0.72 (0.61-0.85)	0.76 (0.56-1.03)	0.54 (0.38-0.75)	
BMI: 25.0-29.9					
Deaths (No.)	353	428	64	64	
HR (95% CI)	1.00[d] (Reference)	0.88 (0.77-1.02)	0.87 (0.66-1.13)	0.72 (0.55-0.95)	.02
BMI: ≥30.0					
Deaths (No.)	162	153	12	9	
HR (95% CI)	1.00 (Reference)	0.91 (0.73-1.14)	0.58 (0.32-1.04)	0.39 (0.20-0.77)	
Health: good					
Deaths (No.)	166	239	44	60	
HR (95% CI)	1.00[d] (Reference)	0.80 (0.65-0.98)	0.84 (0.60-1.18)	0.66 (0.49-0.89)	
Health: poor					
Deaths (No.)	628	661	82	53	
HR (95% CI)	1.00[d] (Reference)	0.85 (0.76-0.95)	0.81 (0.64-1.02)	0.59 (0.44-0.78)	.77
Smoking: yes					
Deaths (No.)	208	206	20	25	
HR (95% CI)	1.00[d] (Reference)	0.87 (0.72-1.06)	0.83 (0.52-1.32)	0.92 (0.61-1.40)	
Smoking: no					
Deaths (No.)	588	695	106	88	
HR (95% CI)	1.00[d] (Reference)	0.82 (0.73-0.92)	0.80 (0.65-0.98)	0.56 (0.45-0.71)	.21
Diabetes: yes					
Deaths (No.)	87	101	15	5	
HR (95% CI)	1.00 (Reference)	0.89 (0.66-1.20)	1.01 (0.58-1.75)	0.63 (0.25-1.57)	
Diabetes: no					
Deaths (No.)	708	799	111	108	
HR (95% CI)	1.00[d] (Reference)	0.82 (0.74-0.91)	0.78 (0.64-0.96)	0.62 (0.51-0.76)	.70

[a]BMI = body mass index; CVD = cardiovascular disease; HR = hazard ratio.
[b]Adjusted for age (age-adjusted time scale) and sex.
[c]*P* value for interaction.
[d]Stratified by sex.

TABLE 5. HRs for Death From All Causes in Subgroups, by Personal Activity Intelligence[a,b]

Subgroup	Personal Activity Intelligence score				*P* value[c]
	0 (n=1280)	≤50 (n=1432)	51-99 (n=199)	≥100 (n=222)	
Men					
Deaths (No.)	672	936	114	170	
HR (95% CI)	1.00 (Reference)	0.86 (0.78-0.95)	0.83 (0.68-1.01)	0.69 (0.58-0.81)	
Women					
Deaths (No.)	530	418	76	20	
HR (95% CI)	1.00 (Reference)	0.77 (0.68-0.88)	0.77 (0.60-0.98)	0.79 (0.51-1.24)	.54
Age ≤70 y					
Deaths (No.)	589	782	112	130	
HR (95% CI)	1.00[d] (Reference)	0.97 (0.87-1.08)	1.02 (0.83-1.24)	0.64 (0.53-0.78)	
Age >70 y					
Deaths (No.)	613	572	78	60	
HR (95% CI)	1.00 (Reference)	0.73 (0.65-0.82)	0.57 (0.45-0.72)	0.57 (0.43-0.75)	.38
Hypertension: yes					
Deaths (No.)	916	978	129	131	
HR (95% CI)	1.00[d] (Reference)	0.79 (0.72-0.87)	0.78 (0.65-0.94)	0.69 (0.57-0.84)	
Hypertension: medication					
Deaths (No.)	80	102	18	8	
HR (95% CI)	1.00 (Reference)	0.94 (0.70-1.27)	0.68 (0.40-1.14)	0.49 (0.24-1.03)	.47
Hypertension: no					
Deaths (No.)	206	274	43	51	
HR (95% CI)	1.00 (Reference)	0.93 (0.77-1.11)	0.98 (0.71-1.37)	0.75 (0.55-1.02)	
BMI: 18.5-24.9					
Deaths (No.)	415	472	74	67	
HR (95% CI)	1.00[d] (Reference)	0.70 (0.61-0.80)	0.73 (0.57-0.94)	0.58 (0.44-0.75)	
BMI: 25.0-29.9					
Deaths (No.)	529	658	95	100	
HR (95% CI)	1.00[d] (Reference)	0.92 (0.82-1.03)	0.87 (0.70-1.08)	0.79 (0.63-0.98)	.05
BMI: ≥30.0					
Deaths (No.)	234	214	20	22	
HR (95% CI)	1.00 (Reference)	0.87 (0.72-1.05)	0.64 (0.40-1.02)	0.66 (0.42-1.04)	
Health: good					
Deaths (No.)	251	368	63	94	
HR (95% CI)	1.00[d] (Reference)	0.82 (0.70-0.97)	0.80 (0.60-1.05)	0.70 (0.55-0.89)	
Health: poor					
Deaths (No.)	949	985	127	96	
HR (95% CI)	1.00 (Reference)	0.84 (0.77-0.92)	0.83 (0.69-1.00)	0.72 (0.58-0.89)	.99
Smoking: yes					
Deaths (No.)	346	341	37	44	
HR (95% CI)	1.00 (Reference)	0.87 (0.75-1.02)	0.97 (0.69-1.36)	1.02 (0.74-1.40)	
Smoking: no					
Deaths (No.)	856	1 013	153	146	
HR (95% CI)	1.00[d] (Reference)	0.83 (0.76-0.91)	0.80 (0.67-0.95)	0.66 (0.55-0.79)	.11
Diabetes: yes					
Deaths (No.)	134	141	21	8	
HR (95% CI)	1.00 (Reference)	0.80 (0.62-1.03)	0.96 (0.60-1.52)	0.65 (0.32-1.35)	
Diabetes: no					
Deaths (No.)	1067	1212	169	182	
HR (95% CI)	1.00[d] (Reference)	0.83 (0.76-0.90)	0.79 (0.67-0.93)	0.71 (0.60-0.83)	.62

[a]BMI = body mass index; CVD = cardiovascular disease; HR = hazard ratio.
[b]Adjusted for age (age-adjusted time scale) and sex.
[c]*P* value for interaction.
[d]Stratified by sex.

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CVD and all-cause mortality is consistent with that from a recent study of a healthy Norwegian population[15] and suggests that the PAI metric is relevant also for individuals with established CVD. It is well established that high-intensity PA improves cardiorespiratory fitness (CRF) in individuals with CVD.[14,17-19] Furthermore, for the same PA volume, high-intensity PA is associated with superior mortality risk reduction compared with moderate-intensity PA.[26] This may be explained by findings showing that high-intensity PA is superior in improving CRF compared with moderate-intensity PA in individuals with and without CVD.[17,27,28] Indeed, higher levels of CRF have been associated with improved cardiovascular risk profile and lower mortality risks in healthy individuals and those with CVD.[29-34] The PAI metric takes into account intensity and time spent performing PA and explains why the PAI metric is a good predictor of mortality risk.

The observation that participants with CVD with a weekly PAI score of 100 had a lower risk of CVD and all-cause mortality, regardless of meeting the PA recommendations or not, indicates that obtaining 100 PAI may be a more accurate and practical way to guide PA levels needed for "optimal" protection against CVD and all-cause mortality compared with today's PA recommendations. Similar to the present study, meeting the PA recommendations has been associated with lower risk of mortality from CVD and all causes in individuals with CVD.[3] However, lack of time has been cited as one of the principle hinders of PA participation.[35] Interestingly, only 40 minutes of high-intensity PA (~85% of the heart rate reserve) is needed to obtain 100 PAI.[16] When it comes to meeting the PA recommendations, one can perform either 150 minutes of moderate-intensity PA or half as much (75 minutes) high-intensity PA.[6] A PAI score of 100 can, therefore, be earned by performing 35 minutes less PA than is currently recommended.

Lack of self-management skills, such as setting personal goals or monitoring PA progress, has been cited as another main reason for impairments to PA participation.[35] To enable self-monitoring of PA, the PAI algorithm has recently been integrated into a wearable device and a freely downloadable app (compatible with most Bluetooth-enabled heart rate monitors). The app analyzes heart rate variations continuously for a week to calculate an individual score, providing instant user feedback on the amount of PAI earned. A PAI score may be shared between patients and their physicians, enabling physicians to encourage their patients to achieve a PAI score of 100. Although the recommendations are beneficial for the health and longevity of patients with CVD, the fact remains that only 17% of patients with CVD are sufficiently physically active.[10,11] Thus, PAI permits for self-management of PA and may be a useful tool in the promotion of PA that may translate into substantial health benefits in patients with CVD.

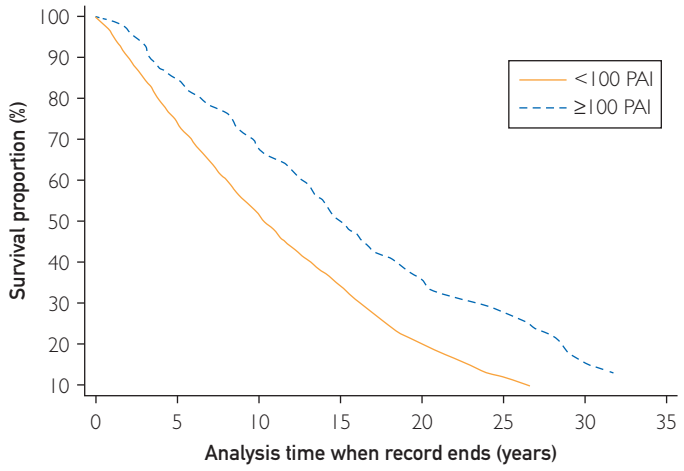

FIGURE 2. Survival curves by Personal Activity Intelligence (PAI) score, adjusted for sex.

Strength and Limitations

The main strengths of the present study are the large sample size, the almost complete follow-up, and the considerable amount of information on potential confounding factors. Nevertheless, the study has some limitations. As with all other observational studies, these findings do not necessarily imply cause and effect. Furthermore, data used to identify patients with CVD and to determine PAI were obtained from a self-reported questionnaire and could be prone to recall bias. Also, we recognize that PA was assessed at baseline only and

that changes over average follow-up of 12.5 years were not considered. However, this may have led to a nondifferential misclassification and could, therefore, underestimate the association between PAI and risk of mortality.[36] We did not have information on objectively measured CRF or left ventricular ejection fraction, which are strong mortality predictors. Furthermore, although the results remained similar after stratification, and adjustment for somatic disease and motion impairment, we cannot exclude the possibility that unknown underlying factors confounded the results. However, these results were not materially changed after exclusion of the first 3 years of mortality follow-up. It is not possible to infer whether the inactive participants are inactive by choice or because of chronic diseases, illnesses, or a debilitating medical condition. Moreover, we did not have information on β-blocker use, which has known effects on the heart and circulation during exercise.[37,38] However, the cardiovascular benefits of exercise training are not diminished by β-blockade.[39] The number of events in subgroups of smokers and participants with diabetes was low. Therefore, the precision of corresponding effect estimates associated with PAI was low, and future studies with larger study samples are needed to draw conclusions related to these groups. Finally, data used in the present study and in the development of the PAI algorithm were derived from the HUNT study cohort, which predominantly consists of white individuals. Its generalizability, therefore, needs to be tested across different races and ethnicities. Thus, the effectiveness of PAI on PA adherence, risk of CVD, and risk of mortality remains to be evaluated in future randomized clinical trials.

CONCLUSION

In this prospective study of individuals with CVD, obtaining a weekly PAI score of at least 100 was associated with lower risk of CVD and all-cause mortality, regardless of whether the current PA recommendations were met.

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Abbreviations and Acronyms: **BMI** = body mass index; **CRF** = cardiorespiratory fitness; **CVD** = cardiovascular disease; **HR** = hazard ratio; **HUNT** = Helseundersøkelsen i Nord-Trøndelag, Nord-Trøndelag Health Study; **MI** = myocardial infarction; **PA** = physical activity; **PAI** = Personal Activity Intelligence

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Potential Competing Interests: Dr Wisløff is the inventor of Personal Activity Intelligence (PAI) and is a shareholder (together with the major shareholder, NTNU Technology Transfer Office, and 3 other enterprises: Femto Inc, Singsaker Holding, and Berre Holding Inc) in a company (Beatstack Inc) that holds the intellectual property rights for PAI. Physical Enterprises Inc, which develops an application that may use data from diverse heart rate monitors, as well as developing wearables that incorporate PAI, owns Beatstack Inc. Due to the potential conflict of interest, we are thankful to the head of science at the Department of Circulation and Medical Imaging, Professor Ola Dale, who monitored adherence to design and statistical analysis in the present study.

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