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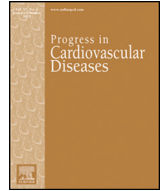
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## Original Research

# Personal activity intelligence and mortality – Data from the Aerobics Center Longitudinal Study



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## ABSTRACT

**Importance:** Personal activity intelligence (PAI) is a novel activity metric that can be integrated into self-assessment heart rate devices, and translates heart rate variations during exercise into a weekly score. Previous studies relating to PAI have been conducted in the same populations from Norway where the PAI metric has been derived, limiting generalizability of the results.

**Objective:** To test whether PAI is associated with total and cause-specific mortality in a large cohort from the United States.

**Design:** Aerobics Center Longitudinal Study (ACLS) – a prospective cohort between January 1974 and December 2002 with a mean follow-up of 14.5 years.

**Setting:** Population-based.

**Participants:** 56,175 relatively healthy participants (26.5% women) who underwent extensive preventive medical examinations at Cooper Clinic (Dallas, TX).

**Exposure:** Personal activity intelligence (PAI) score per week was estimated and divided into 4 groups (PAI scores of 0,  $\leq 50$ , 51–99, and  $\geq 100$ ).

**Main outcomes and measures:** Total and cause-specific mortality.

**Results:** During a median follow-up time of 14.9 (interquartile range, 6.7–21.4) years, there were 3434 total deaths including 1258 cardiovascular (CVD) deaths. Compared with the inactive (0 PAI) group, participants with a baseline weekly  $\geq 100$  PAI had lower risk of mortality: adjusted hazard ratio (AHR), 0.79: 95% CI, 0.71–0.87 for all-cause mortality, and AHR, 0.72: 95% CI, 0.60–0.87 for CVD mortality among men; AHR, 0.85: 95% CI, 0.64–1.12 for all-cause mortality, and AHR, 0.48: 95% CI, 0.26–0.91 for CVD mortality among women. For deaths from ischemic heart disease (IHD), PAI score  $\geq 100$  was associated with lower risk in both men and women (AHR, 0.70: 95% CI, 0.55–0.88). Obtaining  $\geq 100$  weekly PAI was also associated with significantly lower risk of CVD mortality in pre-specified age groups, and in participants with known CVD risk factors. Participants with  $\geq 100$  weekly PAI gained 4.2 (95% CI, 3.5–4.6) years of life when compared with those who were inactive at baseline.

**Conclusions and relevance:** PAI is associated with long-term all-cause, CVD, and IHD, mortality. Clinicians and the general population can incorporate PAI recommendations and thresholds in their physical activity prescriptions

**Abbreviations and acronyms:** ACLS, Aerobics Center Longitudinal Study; BMI, body mass index; BP, blood pressure; CI, confidence interval; CVD, cardiovascular disease; DBP, diastolic blood pressure; HR, hazard ratio; IHD, ischemic heart disease; PA, physical activity; PAI, personal activity intelligence; SBP, systolic blood pressure.

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and weekly physical activity assessments, respectively, to maximize health outcomes.

**Key points: Question:** What is the association between personal activity intelligence (PAI), a novel activity metric, and mortality in a large cohort from the United States?

**Findings:** In this prospective study of 56,175 healthy participants at baseline, followed-up for a mean of 14.5 years,  $\geq 100$  PAI score/week was associated with significant 21% lower risk of all-cause and 30% lower risk of CVD mortality in comparison with inactive people. Participants with  $\geq 100$  PAI/week lived on average 4.2 years longer compared with inactive.

**Meaning:** PAI is associated with long-term all-cause and CVD mortality. Clinicians and general population may incorporate PAI recommendations into weekly physical activity assessments to maximize CVD prevention.

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## Introduction

Adequate levels of physical activity (PA) serve as an effective and inexpensive non-pharmacological therapy that is a primary contributor to: 1) preventing and treating numerous co-morbid conditions, including hypertension, overweight and obesity; 2) lowering the risk of premature all-cause and cardiovascular disease (CVD) mortality; and 3) improving quality of life, functional capacity and mental health.<sup>1–5</sup> Despite the overwhelming evidence demonstrating the health benefits related to PA, physical inactivity has reached pandemic proportions,<sup>6,7</sup> prompting the World Health Organization (WHO) to set a target of 10% relative reduction in the prevalence of inadequate PA by 2025.<sup>8</sup> However, a recent analysis of 1.9 million participants from 358 surveys across 168 countries concluded that the WHO's goal of reducing physical inactivity is unlikely to materialize because of the continual worldwide rise in levels of insufficient PA, particularly in high income countries and among women and minority groups.<sup>9</sup>

The main barriers to participation in PA have been extensively studied and include, but are not limited to, lack of time and the inability to self-manage (i.e., setting personal goals, monitoring PA progress through personalized feedback tailored to individual needs and preferences).<sup>10–12</sup> In keeping with the suggestions for overcoming PA barriers,<sup>11</sup> the Cardiac Exercise Research Group (CERG) ([ntnu.edu/cerg](http://ntnu.edu/cerg)) developed a personalized PA metric, named personal activity intelligence (PAI), with the aim to make it easier to quantify how much PA per week is needed to achieve significant and clinically meaningful reductions in the risk of premature morbidity and mortality from non-communicable diseases.<sup>13</sup> PAI considers an individual's sex, age, and resting and maximal heart rates, and reflects an individual's response to any PA. Importantly, PAI can be integrated into readily available self-assessment heart rate devices and/or Health-Apps and translates heart rate variations over the course of a week into a simple and easily understandable score (0 = inactive, and 100 = active enough). For instance, a score of 100 PAI could be obtained by performing various PA volumes and intensities, using individually preferred PA as long as the heart rate is elevated frequently enough above a certain threshold.<sup>14</sup>

Among individuals ranging from the general population to subgroups of patients with CVD, a PAI score  $\geq 100$  per week at baseline, an increase in PAI score, and a sustained high PAI score over time were found to delay premature all-cause and CVD mortality in a large population of Norwegians.<sup>13–16</sup> However, these findings may not be generalized to other populations because of the relatively homogenous sample of participants from Norway. Therefore, the aim of the present study was to investigate the association between PAI and risk of death in a large United States cohort from the Aerobics Center Longitudinal Study (ACLS) at the Cooper Clinic (Dallas, Texas).<sup>17,18</sup>

## Methods

### Study population

The ACLS is a prospective observational study of men and women who underwent extensive preventive medical examinations from

1974 to 2002.<sup>17</sup> Most of the study participants were college graduates from middle to upper socioeconomic strata, and self-referral as well as referral from an individual's employer or physician were primary mechanisms for ACLS recruitment.

The present study included relatively healthy participants at baseline without a history of cancer ( $n = 1883$ ) or CVD ( $n = 1098$ ). In addition, we excluded participants who had body mass index (BMI) below 18.5 kg/m<sup>2</sup> ( $n = 2222$ ), and those who had <1 year of follow-up ( $n = 1437$ ). A further 6715 participants were excluded owing to missing data on PA. Therefore, a total of 56,175 participants (41,313 men, 14,862 women) were included for analyses of mortality during follow-up (online-only material, eFig. 1). All participants gave informed consent to participate in the study, and Cooper Institute Institutional Review Board reviews and approves the study protocol annually.

### Clinical characteristics: measurements and questionnaire-based information

The clinical examination after an overnight fast included standardized measurements of body height, weight, physical examination, blood pressure (BP) measurements, blood chemistry analyses, and a detailed medical history questionnaire. Resting systolic and diastolic BP (SBP and DBP, respectively) were measured by standardized auscultation methods after at least 5 min of seated rest, and recorded as the average of at least two readings separated by 2 min. Hypertension was defined as SBP/DBP  $\geq 140/90$  mmHg or history of hypertension. Blood chemistries were analysed with automated bioassays in the Cooper Clinic laboratory. Hypercholesterolemia was defined as total cholesterol  $\geq 240$  mg/dl or history of hypercholesterolemia. Diabetes was defined as fasting glucose  $\geq 126$  mg/dl, or current treatment of diabetes, or history of diabetes.

### Personal activity intelligence

Information on leisure time or recreational PA was obtained by self-reported questionnaire and was based on responses to 10 specific activities: walking, jogging, running, treadmill exercise, cycling, stationary cycling, swimming, racquet sports, aerobic dance and other sports-related activities (e.g., basketball, or soccer). Participants were also asked to report frequency and duration for all PA, and speed (average time per mile) for activities such as walking, jogging, running, treadmill exercise and cycling. The intensities of PA were estimated either speed-specific or activity-specific metabolic equivalent (MET) values from the Compendium of Physical Activities.<sup>19,20</sup> PAI scores for each participant were calculated using the responses to PA questions about duration, frequency and intensity.<sup>13,14</sup> The reported intensity of PA was translated to relative intensity (% of heart rate reserve). According to the PAI algorithm described elsewhere,<sup>13</sup> the weekly minutes spent performing PA were obtained by multiplying the average frequency 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. For example, a score of 100 PAI can be obtained by combining 60 weekly minutes of brisk walking, 40 weekly minutes of

cycling, 50 weekly minutes of swimming, 30 weekly minutes of dancing/aerobics, and 20 weekly minutes of running.

#### Assessment of outcomes

Participants were followed from baseline examination until date of death or 31st December 2003, whichever came first. Mortality surveillance was based on the National Death Index (NDI), an accurate method of ascertaining death in observational studies with high sensitivity (96%) and specificity (100%).<sup>21</sup> Death due to CVD was defined using International Classification of Diseases, Ninth Revision (ICD-9) codes 390 to 449.9 before 1999 and Tenth Revision (ICD-10) codes I00 to I78 during 1999–2003.<sup>22</sup> All-cause mortality and death caused by ischemic heart disease (IHD): ICD-9 codes 410 to 414, and ICD-10 codes I20 to I25 were also assessed as outcomes.

#### Statistical analyses

Baseline characteristics were compared using a chi-square test for categorical variables, and regression analyses for continuous variables. To investigate the association between PAI and the risk of mortality, we categorized participants into four groups according to their level of weekly PAI: 0 PAI (inactive),  $\leq 50$  PAI, 51–99 PAI or  $\geq 100$  PAI.<sup>13,14</sup> The inactive group (0 PAI) was used as a reference. The rate of death per 1000 person-years was calculated in each group. We used Cox regression analyses adjusted for several confounders to assess the association between PAI and mortality. The first model included age (years), and year of baseline examination. The second, multi-adjusted, model further included BMI (18.5–24.9, 25.0–29.9, or  $\geq 30.0$  kg/m<sup>2</sup>), smoking status (never, former or current), hypertension (yes or no), diabetes (yes, no), hypercholesterolemia (yes, no), and parental history of CVD (yes, no).<sup>17</sup> Results are reported as adjusted hazard ratios (AHR), and precision of estimates as 95% confidence intervals (CI). The assumption of proportional hazards was examined and satisfied using Schoenfeld residuals, and by addition of time interactions with the covariates.

We also conducted analyses in subgroups of participants, i.e., pre-specified age groups, or those with known CVD risk factors, such as smoking, hypertension, or overweight/obesity. Because of the low number of events and limited statistical power in these subgroup analyses, we pooled men and women together, conditioning on sex in our multi-variable adjusted models. Categorization of participants into  $<100$  PAI and  $\geq 100$  PAI was also performed in assessing the association with mortality. We further categorized the participants into meeting or not meeting the PA recommendations from 2018 PA guidelines for Americans<sup>2</sup> in assessing the association with mortality. Combined associations of PAI and PA recommendations were assessed across four groups, while controlling for various confounders. The following category was used as reference -  $\geq 100$  PAI and meeting the recommendations. Lastly, in a separate analysis, we used Laplace regression,<sup>23,24</sup> adjusted for sex to estimate the years of life gained as the difference in survival years associated with the four different PAI groups.

All statistical tests were two sided and  $P < 0.05$  were considered significant. The statistical analyses were performed using Stata for Windows (Version 15.1, StataCorp LLC, Texas).

#### Results

Baseline characteristics of the participants according to PAI levels are presented in Table 1. Participants with a  $\geq 100$  weekly PAI score (32.7% men and 26.6% women) presented with a healthier phenotype, including a lower prevalence of smoking, diabetes, hypertension and hypercholesterolemia, as well as weighed less, compared to participants with a PAI score  $<100$ .

During a median follow-up time of 15.1 [interquartile range (IQR), 7.5–21.8] years for men, and 12.6 (IQR, 5.3–18.9) years for women, there were 3434 deaths (2872 in men, and 562 in women). The

underlying cause of death was CVD in 1258 cases (1091 in men, 167 in women). Compared with the inactive group, a weekly  $\geq 100$  PAI score was associated with a 21% lower risk of all-cause mortality in men (AHR: 0.79, 95% CI: 0.71–0.87), after adjustment for multiple confounders (Table 2). The corresponding AHR in women was 0.85 (95% CI, 0.64–1.12) for all-cause mortality associated with  $\geq 100$  weekly PAI level.

Participants with a baseline weekly  $\geq 100$  PAI score had significantly lower risk of CVD mortality compared with inactive group: 28% lower risk in men (AHR: 0.72, 95% CI: 0.60–0.87), and 52% lower risk in women (AHR: 0.48, 95% CI: 0.26–0.91) (Table 2). The relative risk reductions were dose dependent over groups ranging from inactive,  $\leq 50$ , 51–99 to the recommended level of  $\geq 100$  PAI ( $P$ -trends  $< 0.01$  for men, and 0.02 for women).

For IHD mortality, a weekly baseline PAI score  $\geq 100$  was associated with a 30% (AHR: 0.70, 95% CI: 0.55–0.88) lower risk compared to inactive group for both men and women ( $P$ -value for sex interaction, 0.93) (Table 3).

In the analyses using participants with a weekly PAI score  $<100$  as referent, those with a  $\geq 100$  PAI had a lower mortality risk. The adjusted HRs for CVD mortality associated with a  $\geq 100$  PAI were 0.74 (95% CI: 0.62–0.88) in men and 0.51 (95% CI: 0.27–0.95) in women. The corresponding HRs for all-cause mortality were 0.80 (95% CI: 0.73–0.89) in men and 0.85 (95% CI: 0.65–1.12) in women (Table 2).

In subgroups of participants, a PAI score of  $\geq 100$ /week was associated with a lower risk of CVD mortality. For example, men and women smokers with a  $\geq 100$  PAI had a 47% lower risk of CVD mortality (AHR: 0.53, 95% CI: 0.33–0.85) compared with the inactive group. The corresponding risk reductions were 36% (AHR: 0.64 95% CI: 0.50–0.82) in overweight/obese, 33% (AHR: 0.67, 95% CI: 0.52–0.85) in hypertensive participants, 26% (AHR: 0.74, 95% CI: 0.57–0.95) in those between the ages of 40 and 55 years, and 25% (AHR: 0.75, 95% CI: 0.58–0.97) among participants  $>55$  years (online-only material, eFig. 2).

The results of combined analyses between PAI and PA recommendations show that both  $\geq 100$  weekly PAI and meeting the new PA recommendations were associated with a lower mortality risk. Compared with the reference group (i.e.,  $\geq 100$  weekly PAI and meeting the recommendations), participants with  $\geq 100$  PAI and not meeting the recommendations did not have a significantly high risk of all-cause mortality (AHR: 1.00, 95% CI: 0.84–1.18). The corresponding AHR for CVD mortality was 0.90 (95% CI: 0.65–1.24). In participants who met the PA recommendations but had  $<100$  weekly PAI, the AHRs were 0.83 (95% CI: 0.47–1.48) for all-cause mortality and 0.63 (95% CI: 0.20–1.98) for CVD mortality, albeit fewer events (Table 4).

Compared with the inactive group, participants with  $\geq 100$  weekly PAI had 4.2 (95% CI: 3.5–4.6) years of life gained (Fig. 1). The corresponding number of years gained were 3.8 (95% CI: 2.0–5.7) among women and 4.2 (95% CI: 3.4–5.1) among men (data not shown).

#### Discussion

In the current study, using the ACLS prospective cohort from the United States, we found that obtaining  $\geq 100$  weekly PAI was associated with a significantly lower risk of premature mortality in apparently healthy men and women; this association was even more apparent in disease-specific subgroups.

Previous studies<sup>13–16</sup> on PAI have been conducted in larger cohorts from Norway, where the PAI metric was initially developed. While these initial findings were compelling, limitations in generalizability to populations with differing characteristics warrant further investigation. In this context, the current study is the first to convincingly link PAI to mortality in a large cohort from the United States. As such, the findings of the present study extend our knowledge about PAI and mortality, and provide further evidence of the validity of a simple PA metric (i.e., PAI).

The main finding of the current study is that a weekly PAI score of  $\geq 100$  was associated with lower risk of all-cause and CVD mortality in

**Table 1**  
Baseline characteristics of study participants (n = 56,175).

	Men				P value <sup>a</sup>	Women				P value <sup>a</sup>
	Inactive (n = 21,025)	≤50 (n = 3489)	51–99 (n = 3288)	≥100 (n = 13,511)		Inactive (n = 8044)	≤50 (n = 1378)	51–99 (n = 1490)	≥100 (n = 3950)	
Age, mean (SD), y	44.2 (10.1)	46.6 (10.1)	45.6 (10.5)	43.1 (9.3)	<0.01	44.5 (11.7)	45.7 (11.3)	46.1 (10.4)	42.5 (10.5)	<0.01
Body mass index, no. (%)										
18.5–24.9	6906 (32.9)	1057 (30.3)	1134 (34.5)	6236 (46.2)	<0.01	5591 (69.5)	913 (66.2)	1073 (72.0)	3222 (81.5)	<0.01
25.0–29.9	10,076 (47.9)	1669 (47.8)	1603 (48.7)	6017 (44.5)		1556 (19.3)	311 (22.6)	297 (19.9)	579 (14.7)	
≥30.0	4043 (19.2)	763 (21.9)	551 (16.8)	1258 (9.3)		897 (11.2)	154 (11.2)	120 (8.1)	149 (3.8)	
Systolic BP, mean (SD), mm Hg	122.6 (14.0)	123.2 (14.3)	122.2 (13.7)	121.8 (13.3)	<0.01	115.2 (16.3)	114.6 (15.6)	114.2 (14.9)	112.2 (14.1)	<0.01
Diastolic BP, mean (SD), mm Hg	82.0 (9.8)	82.5 (10.0)	81.7 (9.6)	80.6 (9.3)	<0.01	76.8 (10.1)	76.8 (9.7)	76.6 (9.5)	75.4 (9.4)	<0.01
Hypertension status, no. (%) <sup>b</sup>										
Yes	7160 (34.1)	1318 (37.8)	1130 (34.4)	3801 (28.1)	<0.01	1694 (21.1)	282 (20.5)	285 (19.1)	551 (13.9)	<0.01
No	13,865 (65.9)	2171 (62.2)	2158 (65.6)	9710 (71.9)		6350 (78.9)	1096 (79.5)	1205 (80.9)	3399 (86.1)	
Smoking status, no. (%)										
Never	9911 (47.1)	1956 (56.1)	1774 (54.0)	7724 (57.2)	<0.01	5442 (67.6)	999 (72.5)	1062 (71.3)	2742 (69.4)	<0.01
Former	6221 (29.6)	1031 (29.6)	1060 (32.2)	4334 (32.1)		1689 (21.0)	291 (21.1)	344 (23.1)	957 (24.2)	
Current	4893 (23.3)	502 (14.3)	454 (13.8)	1453 (10.7)		913 (11.4)	88 (6.4)	84 (5.6)	251 (6.4)	
Fasting glucose, mean (SD), mmol/L	5.7 (1.2)	5.6 (1.1)	5.6 (0.9)	5.5 (0.7)	<0.01	5.3 (1.1)	5.2 (1.0)	5.2 (1.0)	5.0 (0.9)	<0.01
Diabetes, No. (%) <sup>c</sup>										
Yes	1558 (7.4)	211 (6.1)	214 (6.5)	509 (3.8)	<0.01	322 (4.0)	60 (4.4)	75 (5.0)	149 (3.8)	<0.01
No	19,467 (92.6)	3278 (93.9)	3074 (93.5)	13,002 (96.2)		7722 (96.0)	1318 (95.6)	1415 (95.0)	3801 (96.2)	
Total cholesterol, mean (SD), mmol/L	5.5 (1.1)	5.4 (1.0)	5.4 (1.0)	5.3 (1.1)	<0.01	5.3 (1.1)	5.3 (1.0)	5.2 (1.0)	5.0 (0.9)	<0.01
Hypercholesterolemia, no. (%) <sup>d</sup>										
Yes	5915 (28.1)	1082 (31.0)	971 (29.5)	3351 (24.8)	<0.01	1768 (22.0)	354 (25.7)	356 (23.9)	730 (18.5)	<0.001
No	15,110 (71.9)	2407 (69.0)	2317 (70.5)	10,160 (75.2)		6276 (78.0)	1024 (74.3)	1134 (76.1)	3220 (81.5)	
Parental cardiovascular disease, No. (%) <sup>e</sup>										
Yes	5441 (25.9)	947 (27.1)	908 (27.6)	3414 (25.3)	0.01	1998 (24.8)	386 (28.0)	432 (29.0)	902 (22.8)	<0.01
No	15,584 (74.1)	2542 (72.9)	2380 (72.4)	10,097 (74.7)		6046 (75.2)	992 (72.0)	1058 (71.0)	3048 (77.2)	

<sup>a</sup>For linear trend, regression analyses were used for continuous variables;  $\chi^2$  tests were used for proportions of categorical variables.

<sup>b</sup>Defined as systolic blood pressure  $\geq 140$  mm Hg and/or diastolic blood pressure  $\geq 90$  mm Hg and/or history of hypertension.

<sup>c</sup>Defined as fasting glucose  $\geq 126$  mg/dl (7.0 mmol/L), current therapy with insulin, or history of diabetes.

<sup>d</sup>Defined as total cholesterol  $\geq 240$  mg/dl (6.3 mmol/L) or history of hypercholesterolemia.

<sup>e</sup>Parental history of premature coronary heart disease and/or stroke.

individuals from the United States, consistent with studies in healthy Norwegian cohorts,<sup>13,14,16</sup> suggesting that the PAI activity metric is relevant in diverse populations. The results on the association between PAI and IHD mortality are novel, also demonstrating a lower risk associated with a  $\geq 100$  PAI/week.

The new PA guidelines for Americans<sup>2</sup> suggest that adults should engage in at least 150–300 weekly minutes of moderate intensity PA or 75–150 weekly minutes of vigorous aerobic intensity PA, or an equivalent

combination of moderate or vigorous intensity exercise. Our results of combined analyses of PAI and PA recommendations suggest that a target score of  $\geq 100$  weekly PAI may fit well with these new recommendations, as PAI offers individuals with a variety of options and choices relating to quality, quantity, and intensity of PA. However, the observation that individuals who did not fulfill the PA guidelines for Americans, but still obtained  $\geq 100$  weekly PAI, had similar mortality risk as those achieving the recommendation with  $\geq 100$  weekly PAI. This finding suggests that

**Table 2**  
Hazard ratios of death by PAI.

PAI	Men					Women				
	Person-years	Deaths	Rate	HR (95% CI) <sup>a</sup>	HR (95% CI) <sup>b</sup>	Person-years	Deaths	Rate	HR (95% CI) <sup>a</sup>	HR (95% CI) <sup>b</sup>
All-causes										
Inactive	358,121	2044	5.7	1.00 (Ref.)	1.00 (Ref.)	119,856	421	3.5	1.00 (Ref.)	1.00 (Ref.)
≤50	42,004	184	4.4	0.93 (0.80–1.09)	0.98 (0.84–1.14)	15,185	42	2.8	0.83 (0.60–1.14)	0.93 (0.68–1.29)
51–99	42,807	167	3.9	0.76 (0.65–0.89)	0.82 (0.70–0.97)	15,721	37	2.4	0.93 (0.66–1.30)	1.05 (0.74–1.48)
≥100	179,451	477	2.7	0.67 (0.60–0.74)	0.79 (0.71–0.87)	42,622	62	1.5	0.74 (0.56–0.97)	0.85 (0.64–1.12)
				<i>p</i> -trend < 0.001	<i>p</i> -trend < 0.001				<i>p</i> -trend = 0.03	<i>p</i> -trend = 0.34
<100	422,932	2395	5.4	1.00 (Ref.)	1.00 (Ref.)	150,762	500	3.3	(Ref.)	(Ref.)
≥100	179,451	477	2.7	0.69 (0.63–0.77)	0.80 (0.73–0.89)	42,622	62	1.5	0.76 (0.58–0.99)	0.85 (0.65–1.12)
CVD										
Inactive	358,121	804	2.2	1.00 (Ref.)	1.00 (Ref.)	119,856	137	1.1	1.00 (Ref.)	1.00 (Ref.)
≤50	42,004	80	1.9	1.06 (0.84–1.34)	1.11 (0.88–1.41)	15,185	10	0.7	0.56 (0.30–1.08)	0.67 (0.35–1.29)
51–99	42,807	55	1.3	0.63 (0.48–0.83)	0.70 (0.53–0.93)	15,721	9	0.6	0.75 (0.38–1.49)	0.89 (0.45–1.77)
≥100	179,451	152	0.8	0.56 (0.47–0.67)	0.72 (0.60–0.87)	42,622	11	0.3	0.43 (0.23–0.80)	0.48 (0.26–0.91)
				<i>p</i> -trend < 0.001	<i>p</i> -trend < 0.001				<i>p</i> -trend = 0.004	<i>p</i> -trend = 0.02
<100	442,932	939	2.1	1.00 (Ref.)	1.00 (Ref.)	150,762	156	1.0	(Ref.)	(Ref.)
≥100	179,451	152	0.8	0.58 (0.49–0.69)	0.74 (0.62–0.88)	42,622	11	0.3	0.46 (0.25–0.86)	0.51 (0.27–0.95)

CI, confidence interval; HR, hazard ratio; PAI, personal activity intelligence.

Rate per 1000 person-year.

<sup>a</sup> Adjusted for age and examination year.

<sup>b</sup> Adjusted for age, examination year, smoking (never, former, current), body mass index (normal-weight, overweight, obese), hypertension (normal, hypertensive), diabetes (yes, no), hypercholesterolemia (yes, no), and parental history of cardiovascular disease (yes, no).

**Table 3**  
Hazard ratios of death from ischemic heart disease by PAI.

PAI	Person-years	Deaths	Rate	HR (95% CI) <sup>a</sup>	HR (95% CI) <sup>b</sup>
Inactive	477,977	525	1.2	1.00 (Ref.)	1.00 (Ref.)
≤50	57,189	52	0.9	0.98 (0.73–1.31)	1.04 (0.78–1.39)
51–99	58,527	37	0.6	0.71 (0.51–0.99)	0.80 (0.57–1.12)
≥100	222,073	92	0.4	0.55 (0.44–0.69)	0.70 (0.55–0.88)
				<i>p</i> -trend < 0.001	<i>p</i> -trend < 0.001
<100	593,693	614	1.1	1.00 (Ref.)	1.00 (Ref.)
≥100	222,073	92	0.4	0.56 (0.45–0.71)	0.71 (0.57–0.89)

CI, confidence interval; HR, hazard ratio; PAI, personal activity intelligence.

Rate per 1000 person-years.

<sup>a</sup> Adjusted for age, examination year and stratified by sex.

<sup>b</sup> Adjusted for age, examination year, smoking (never, former, current), body mass index (normal-weight, overweight, obese), hypertension (normal, hypertensive), diabetes (yes, no), hypercholesterolemia (yes, no), parental history of cardiovascular disease (yes, no), and stratified by sex.

PAI is an easier metric to guide people when enough PA has been undertaken for risk reduction against all-cause and CVD mortality.

With advances in technology and the advent of wearable devices, it is much easier now to track and self-monitor PA. The PAI metric has recently been integrated into wearable devices, and is available to the public worldwide through a freely downloadable app that is compatible with most Bluetooth-enabled heart rate monitors. The app analyses heart rate variations continuously for a week to calculate an individual personalized score, providing instant user feedback on the amount of PAI earned. A PAI score may be shared between patients and their physicians in clinical practice, enabling physicians to encourage their patients to achieve target scores of ≥100 PAI. Although, the strongest effects occur with PAI ≥100, it should be noted that progressive benefits were observed across the spectrum of PAI; men with PAI 50–99 had significant lower risk of mortality, with trends noted in women for CVD mortality and among men and women for death caused by IHD. These results could potentially be utilized in the promotion of effective PA for the primary and secondary prevention of CVD.<sup>25</sup> Overall, these findings reinforce the message that “moving more and sitting less”, by any means necessary, has tremendous health benefits.<sup>26</sup> This message has also been adopted by the new PA guidelines for Americans.<sup>2</sup>

**Strength and limitations**

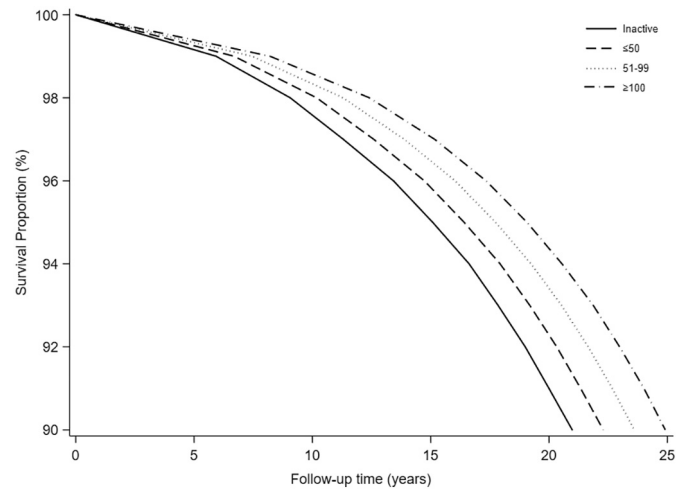
The main strengths of the present study include a relatively large population-based cohort of healthy men and women, the long-term follow-up time, a large set of major outcomes studied, and information on a broad range of confounding factors. Moreover, we excluded participants with a history of CVD and cancer, those with a BMI <18.5 kg/m<sup>2</sup>, and those who died during the first year of follow-up, thus minimizing

**Table 4**  
Hazard Ratios for combined association between PAI and physical activity.

All-cause mortality	≥100 PAI		<100 PAI	
	Deaths	HR (95% CI) <sup>a</sup>	Deaths	HR (95% CI) <sup>a</sup>
Recommended PA (MET-minutes/week)				
Yes (≥1125)	325	1.00 (Reference)	12	0.83 (0.47–1.48)
No (0–1124)	214	1.00 (0.84–1.18)	2883	1.24 (1.10–1.39)
CVD mortality				
Yes (≥1125)	102	1.00 (Reference)	3	0.63 (0.20–1.98)
No (0–1124)	61	0.90 (0.65–1.24)	1092	1.35 (1.09–1.66)

CI, confidence interval; HR, hazard ratio; PAI, personal activity intelligence, PA, physical activity.

<sup>a</sup> Adjusted for age, examination year, smoking (never, former, current), body mass index (normal-weight, overweight, obese), hypertension (normal, hypertensive), diabetes (yes, no), hypercholesterolemia (yes, no), parental history of cardiovascular disease (yes, no), and stratified by sex.



**Fig. 1.** Survival curves by personal activity intelligence. PAI, personal activity intelligence. Participants were classified into four PAI groups: Inactive (0 PAI), ≤50 PAI, 51–99 PAI or ≥100 weekly PAI.

the likelihood of underlying subclinical disease. The study, however, also has some limitations. Data used to estimate PAI was self-reported and, therefore, prone to information bias. However, the nature of misclassification in prospective studies is most likely to be non-differential in relation to future disease, and therefore likely to yield underestimates of the true effects. The ACLS study population is comprised of well-educated, non-Hispanic whites from middle to upper socioeconomic strata, and therefore, may have some similarities with the Norwegian population from which PAI was developed. However, physiologic characteristics of participants from the ACLS were similar with the representative population groups<sup>27</sup> and other large studies from the United States.<sup>28,29</sup> Nonetheless, the generalizability of the PAI metric in different races and ethnicities with varying CVD risk still warrants additional investigations. Although, we studied a relatively healthy population and analyses were controlled for possible known confounders, unknown underlying factors and lack of data especially about diet and medications use may have introduced some residual and unmeasured confounding. Despite the large number of study participants, the number of events in certain subgroups was low (e.g., age group <40 years, and those with <100 PAI and meeting the PA recommendations), affecting the precision of corresponding effect estimates. Therefore, cautious interpretation of results in these subgroups is necessary. Finally, the participants could have changed their PA status during the follow-up time. However, this may be a potential strength of our study, indicating that a single measure of PAI at baseline is associated with long-term all-cause and CVD mortality.

**Clinical recommendations and impact**

Clinicians have typically experienced considerable difficulty motivating patients to perform adequate PA to prevent CVD and prolong survival, as well as explaining exactly how long and intense PA needs to be to produce maximal benefits.<sup>5,30</sup> Additionally, although the 2018 PA guidelines<sup>2</sup> represent an improvement and somewhat simplification compared to the previous version, individuals continue to remain uncertain on the volume of moderate or vigorous PA, and exactly how to define these PA intensities. Using the PAI, clinicians can easily recommend that patients obtain at least 100 PAI for most favourable protection against all-cause and CVD mortality, but can also mention that significant benefits also occur at the 50–99 PAI level. This strategy may be particularly useful in transitioning those who are sedentary to some level of PA that have significant health benefits.<sup>26</sup> Using a simplified approach that is validated in Norway and United States populations,

as well as in sub-populations with multiple co-morbidities, clinicians and the public can now be confident with these PAI recommendations and thresholds for adequate PA, potentially for the primary and secondary prevention of CVD.<sup>5,25</sup>

## Conclusion

In summary, PAI is associated with long-term all-cause, CVD and IHD mortality in a large United States cohort, consistent with previous findings in a larger Norwegian cohort. Clinicians and the general population can incorporate PAI recommendations and thresholds in their PA prescriptions and weekly PA assessments, respectively, to maximize CVD prevention and improve prognosis.

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.pcad.2020.05.005>.

## Statement of conflict of interest

Professor Wisløff is the inventor of PAI, and scientific advisor of a company (PAI Health Inc.) that holds the IP rights for PAI and develops applications that utilize data from diverse heart rate monitors to display PAI for users. Due to the potential conflict of interest, Professor Wisløff was not involved in the data acquisition and statistical analyses of the data in the current study. There are no further disclosures or potential conflicts of interest to report.

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