

# Personalized Activity Intelligence (PAI) for Prevention of Cardiovascular Disease and Promotion of Physical Activity

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## ABSTRACT

**PURPOSE:** To derive and validate a single metric of activity tracking that associates with lower risk of cardiovascular disease mortality.

**METHODS:** We derived an algorithm, Personalized Activity Intelligence (PAI), using the HUNT Fitness Study (n = 4631), and validated it in the general HUNT population (n = 39,298) aged 20-74 years. The PAI was divided into three sex-specific groups ( $\leq 50$ , 51-99, and  $\geq 100$ ), and the inactive group (0 PAI) was used as the referent. Hazard ratios for all-cause and cardiovascular disease mortality were estimated using Cox proportional hazard regressions.

**RESULTS:** After >1 million person-years of observations during a mean follow-up time of 26.2 (SD 5.9) years, there were 10,062 deaths, including 3867 deaths (2207 men and 1660 women) from cardiovascular disease. Men and women with a PAI level  $\geq 100$  had 17% (95% confidence interval [CI], 7%-27%) and 23% (95% CI, 4%-38%) reduced risk of cardiovascular disease mortality, respectively, compared with the inactive groups. Obtaining  $\geq 100$  PAI was associated with significantly lower risk for cardiovascular disease mortality in all prespecified age groups, and in participants with known cardiovascular disease risk factors (all *P*-trends <.01). Participants who did not obtain  $\geq 100$  PAI had increased risk of dying regardless of meeting the physical activity recommendations.

**CONCLUSION:** PAI may have a huge potential to motivate people to become and stay physically active, as it is an easily understandable and scientifically proven metric that could inform potential users of how much physical activity is needed to reduce the risk of premature cardiovascular disease death.

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Low levels of physical activity have reached pandemic proportions, contributing to >5 million deaths each year worldwide.<sup>1,2</sup> Inadequate physical activity not only results in increased individual health burden,<sup>3</sup> but also contributes to tremendous health care expenditures for the society.<sup>4,5</sup> Therefore, promotion of physical activity is needed throughout the health care system.<sup>6,7</sup>

Current recommendations of physical activity suggest that adults should engage in at least 150 minutes of moderate-intensity activity or 75 minutes of vigorous-intensity activity per week, or any combination of activity

that approximates the same total energy expenditure.<sup>8-10</sup> Recent studies have also shown significant benefits at activity levels as low as half of the recommended quantity.<sup>11,12</sup>

Evolving evidence suggests that cardiorespiratory fitness outperforms physical activity as a predictor of future health.<sup>13-15</sup> Moreover, several studies suggest that people with established cardiovascular disease risk factors, such as high body mass index (BMI), hypertension, or diabetes, but with high cardiorespiratory fitness, have highly attenuated risk of cardiovascular disease and premature mortality.<sup>13,14,16</sup>

A major challenge in activity counseling and promotion of physical activity is to provide clear feedback to individuals with personalized and meaningful information that motivate individuals to increase or sustain physical activity.<sup>17,18</sup> Goals such as “10,000 steps per day” or “30 minutes of activity per day” tend to be vague and misleading, as they do not reflect the body’s response to each activity. The most personalized, accurate way to track and measure the body’s response to activity is through monitoring a person’s heart rate.<sup>9</sup> Unlike all other physical activity metrics, such as distance walked, number of steps, frequency or duration of activity, heart rate changes reflect the body’s response to physical activity regardless of the type of activity performed. However, there has never been a simple way to convert heart rate changes during physical activity into a meaningful metric for understanding how much activity or exercise is necessary, and what intensity level is needed to achieve optimal health results.

Therefore, the aim of the current study was to develop a new single metric (Personalized Activity Intelligence [PAI]) that can be integrated in self-assessment heart rate devices, and defines a weekly beneficial heart rate pattern during physical activity. Further, we aimed to assess whether PAI could translate into reduced long-term risk of premature cardiovascular disease and all-cause mortality.

## METHODS

### Derivation Cohort

The derivation cohort to develop the PAI algorithm consisted of participants in the HUNT Fitness Study (2006-2008).<sup>19,20</sup> In total, 4631 healthy subjects completed an individualized peak oxygen uptake ( $VO_{2peak}$ ) test running on a treadmill.<sup>19</sup>

### Clinical Examinations

$VO_{2peak}$  was measured by ergospirometry (MetaMax II; Cortex Biophysik GmbH, Leipzig, Germany). Maximal

heart rate was defined as the highest heart rate obtained during peak exercise. Details about the test procedures are presented elsewhere.<sup>19</sup> Trained nurses conducted other clinical examinations of standardized measurements of height, weight, blood pressure, and resting heart rate.

## CLINICAL SIGNIFICANCE

- Personalized Activity Intelligence (PAI), an easily understandable metric of physical activity, is associated with reduced risk of dying prematurely from all causes and from cardiovascular disease.
- Obtaining a score of 100 PAI over a week gave similar reduction in risk of dying regardless of meeting the current recommendation for physical activity or not.
- PAI could be incorporated in self-assessment heart rate devices to self-monitor the activity levels needed to achieve maximum health benefits.

## Personalized Activity Intelligence (PAI)

The purpose of the model design was to develop a generic algorithm suitable for real-time implementation on a device connected to, or integrated with, a continuous heart rate sensor. Previous studies on the same derivation cohort showed that a nonexercise model could be used to estimate cardiorespiratory fitness for individuals.<sup>21-23</sup> The fundamental basis of PAI is to exchange the self-reported exercise level (intensity, duration, and frequency) from these studies<sup>21-24</sup> with measured heart rate. Further details of mathematical modeling to derive PAI are presented in the

[supplementary materials](#) available online.

## Validation Cohort

The validation cohort consisted of 70,535 participants aged 20-74 years in the first wave of HUNT (1984-86). After making multiple exclusions (see [supplementary materials](#), available online), a total of 39,298 (20,029 women and 19,269 men) were included in the analyses of this study ([Supplementary Figure 1](#), available online). We compared the 39,298 participants who were included with the 31,237 participants who were excluded. As expected, the excluded participants were older and had worse cardiovascular risk profiles than those who were included in the study ([Supplementary Table 1](#), available online).

## Questionnaire-Based Information

For the validation cohort, information on exercise habits were collected through a questionnaire containing questions about frequency, duration, and intensity of physical activity over a normal week. Numbers of exercise sessions were multiplied with the median duration to obtain an estimate of total time spent on exercise per week. Intensity of exercise stated as “How hard do you exercise?” contained three response options (“no sweat or heavy breath,” “heavy breath and some sweat,” and “push myself to exhaustion”). Based on previous studies<sup>12,23,25,26</sup> from our group using the HUNT Fitness population, these relative intensities correspond to 44%, 73%, and 83% of heart rate reserve (maximal heart rate – resting heart rate), respectively,

which was used in the analysis. Questionnaire data were also collected for smoking status (smoker, nonsmoker), education (total years of education), alcohol consumption (number of alcoholic drinks over 2 weeks), and a wide range of present diseases.

## Outcomes

The primary outcome of the validation study was death from cardiovascular disease (International Classification of Diseases, Ninth Revision codes 390–459, International Classification of Diseases, Tenth Revision codes I00–99), and secondary outcome was death from all-causes. Data were linked to the National Cause of Death Registry through the 11-digit Norwegian personal identification number, allowing for virtually complete follow-up. All participants provided a written informed consent, and the study was approved by the regional committee for medical research ethics.

## Statistical Analyses

The PAI over 1 week was calculated for each participant in the validation cohort on the basis of the algorithm provided from the derivation cohort. PAI was divided into three groups ( $\leq 50$ , 51–99, and  $\geq 100$  PAI), and the inactive group (0 PAI) was used as the reference category. Person-years were calculated from attendance date in HUNT-1 until date of death or end of follow-up on December 31, 2013, whichever came first. Rate of death for each PAI category was calculated per 1000 person-years. We then assessed hazard ratios (HR) with 95% confidence intervals (CI) for death associated with PAI categories by Cox proportional hazard regression models. The age-adjusted models included attained age as the time scale while the multi-adjusted models further included smoking, BMI, hypertension, alcohol consumption, and education. We found no evidence for violation of the proportional hazards assumption examined by Schoenfeld residuals. In secondary analysis, we stratified participants by age group at baseline (<40, 40–55, or >55 years) and presence of overweight/obesity (BMI  $\geq 25$  kg·m<sup>-2</sup>), smoking status, and hypertension (blood pressure  $\geq 140/90$  mm Hg or antihypertensive medications).

We performed sensitivity analyses to assess the robustness of our findings by excluding the first 3 years of follow-up. In another analysis, we categorized the PAI into two groups, <100 and  $\geq 100$ , and divided participants according to physical activity recommendations from AHA,<sup>10</sup> and assessed the isolated and combined associations of the PAI and physical activity recommendations after controlling for various confounders. In a separate analysis, we calculated years of life lost as a difference between the adjusted median life expectancy for PAI groups,<sup>27</sup> where survival probabilities at each age for each individual were calculated, and then averaged to obtain an overall summary curve. All statistical tests were two sided and considered significant at

$P < .05$ . All analyses were conducted using Stata (version 13.1, StataCorp LLP, College Station, Texas).

## RESULTS

The distribution of clinical and demographic characteristics of participants in the validation cohort is presented in **Table 1**. Participants with  $\geq 100$  PAI corresponding to 40 minutes of high-intensity ( $\sim 85$  % heart rate reserve) or 60 minutes of moderate-intensity activity ( $\sim 75$  % heart rate reserve) in a week (26.6% men and 14.9% women) appeared to have a healthier lifestyle: lower prevalence of hypertension and smoking, and weighed less compared with other participants. The derivation cohort of HUNT Fitness Study was more active, had lower prevalence of hypertension and smoking compared with the validation cohort (**Supplementary Table 2**, available online).

After 1,029,684 person-years of observations during a mean follow-up of 26.2 (SD 5.9) years in the validation cohort, there were 10,062 deaths, including 3867 deaths (2207 men and 1660 women) from cardiovascular disease.

In general, men and women with a PAI level  $\geq 100$  had 17% (95% CI, 7%–27%) and 23% (95% CI, 4%–38%) reduced risk of cardiovascular disease mortality, respectively, compared with the inactive groups (**Table 2**). The corresponding risk reduction for all-cause mortality was 13% (95% CI, 6%–20%) and 17% (95% CI, 6%–26%) for men and women, respectively. No further risk reductions or loss of benefit were observed beyond obtaining a weekly 100 PAI (data not shown).

## Subgroup Analyses

Obtaining  $\geq 100$  PAI was associated with a significantly lower risk for cardiovascular disease mortality compared with inactive groups in all prespecified age groups for men (<40 years: HR, 0.59 [95% CI, 0.38–0.92]; 40–55 years: HR, 0.62 [95% CI, 0.48–0.79]; >55 years: HR, 0.80 [95% CI, 0.69–0.93]) and women (40–55 years: HR, 0.35 [95% CI, 0.19–0.65]; and >55 years: HR, 0.70 [95% CI, 0.55–0.89]) (**Figure 1**).

Participants with presence of known cardiovascular disease risk factors, such as smoking, hypertension, or overweight/obese, showed similar risk reductions by obtaining  $\geq 100$  PAI compared with the inactive groups (**Figure 2**). For example, men and women smokers with  $\geq 100$  PAI had 21% (95% CI, 4%–35%) and 42% (95% CI, 10%–63%) lower risk, respectively, of cardiovascular disease mortality compared with the inactive group; while the corresponding risk reductions were 26% (95% CI, 14%–35%) and 37% (95% CI, 18%–51%) in hypertensive men and women, and 22% (95% CI, 8%–33%) and 39% (95% CI, 18%–55%) in overweight/obese men and women, respectively. Similar patterns were observed for all-cause mortality (**Figure 2**). The results of the analyses stratified by hypertension or diabetes status at baseline were not substantially different from the main analyses, where

**Table 1** Baseline Characteristics of Study Participants in Validation Cohort (n = 39,298)

	Men				P Value*	Women				P Value*
	Inactive (n = 8222)	≤50 (n = 4187)	51-99 (1730)	≥100 (5130)		Inactive (n = 7766)	≤50 (n = 7050)	51-99 (n = 2234)	≥100 (n = 2979)	
Age, mean (SD), y	41.6 (13.4)	48.1 (14.7)	42.7 (13.6)	39.4 (13.2)	<.001	42.0 (13.7)	46.1 (14.8)	41.2 (13.6)	37.7 (12.0)	<.001
Body mass index, mean (SD), kg/m <sup>2</sup>										
<18.5	17.8 (0.6)	17.5 (0.5)	18.0 (0.5)	17.9 (0.5)		17.7 (0.6)	17.7 (0.6)	17.9 (0.5)	17.8 (0.6)	
18.5-24.9	22.7 (1.5)	22.9 (1.5)	22.9 (1.4)	22.9 (1.3)	<.001	22.1 (1.7)	22.2 (1.6)	22.1 (1.6)	22.0 (1.5)	<.001
≥25.0	27.8 (2.5)	27.6 (2.3)	27.4 (2.2)	27.2 (2.1)		28.9 (3.8)	28.6 (3.4)	28.1 (3.0)	28.1 (3.2)	
Hypertension status, n (%)†										
Yes	3790 (46.1)	2256 (53.9)	828 (47.9)	2137 (61.7)		2537 (32.7)	2861 (40.6)	628 (28.1)	672 (22.6)	
No	4432 (53.9)	1931 (46.1)	902 (52.1)	2993 (58.3)	<.001	5229 (67.3)	4189 (59.4)	1606 (71.9)	2307 (77.4)	<.001
Smoking status, n (%)										
Yes	3862 (47.0)	1618 (38.6)	519 (30.0)	1170 (22.8)		3365 (43.3)	2285 (32.4)	720 (32.2)	828 (27.8)	
No	4360 (53.0)	2569 (61.4)	1211 (70.0)	3960 (77.2)	<.001	4401 (56.7)	4765 (67.6)	1514 (67.8)	2151 (72.2)	<.001
Alcohol consumption, n (%)‡										
Abstainer	373 (4.5)	261 (6.2)	84 (4.9)	214 (4.2)		847 (10.9)	859 (12.2)	173 (7.7)	190 (6.4)	
Zero	2656 (32.3)	1532 (36.6)	507 (29.3)	1535 (29.9)		4124 (53.1)	3758 (53.3)	1079 (48.3)	1376 (46.2)	
1-4 times	4380 (53.3)	2056 (49.1)	997 (57.6)	2974 (58.0)	<.001	2496 (32.1)	2226 (31.5)	910 (40.7)	1296 (43.5)	<.001
5-10 times	411 (5.0)	172 (4.1)	92 (5.3)	241 (4.7)		119 (1.5)	95 (1.4)	43 (1.9)	68 (2.3)	
>10 times	402 (4.9)	166 (4.0)	50 (2.9)	166 (3.2)		180 (2.3)	112 (1.6)	29 (1.3)	49 (1.6)	
Education, n (%)										
<10 y	4333 (52.7)	2372 (56.7)	733 (42.4)	1849 (36.0)		4793 (61.7)	4433 (62.9)	1130 (50.6)	1212 (40.7)	
10-12 y	3066 (37.3)	1279 (30.5)	644 (37.2)	2132 (41.6)	<.001	2357 (30.4)	1959 (27.8)	807 (36.1)	1184 (39.7)	<.001
≥13 y	823 (10.0)	536 (12.8)	353 (20.4)	1149 (22.4)		616 (7.9)	658 (9.3)	297 (13.3)	583 (19.6)	
Physical activity habits, n (%)										
Frequency										
Inactive/<Once a wk	8222 (100)	—	—	—		7766 (100)	—	—	—	
Once a wk	—	2545 (60.8)	1442 (83.3)	800 (15.6)		—	3685 (52.3)	1512 (67.7)	368 (12.4)	
2-3 times a wk	—	1038 (24.8)	—	3347 (65.2)	<.001	—	2520 (35.7)	1 (0.04)	2092 (70.2)	<.001
Almost everyday	—	604 (14.4)	288 (16.7)	983 (19.2)		—	845 (12.0)	721 (32.2)	519 (17.4)	
Duration per session										
<30 min	—	2473 (59.1)	34 (2.0)	540 (10.5)		—	4434 (62.9)	25 (1.1)	688 (23.1)	
≥30 min	—	1714 (40.9)	1696 (98.0)	4590 (89.5)	<.001	—	2616 (37.1)	2209 (98.9)	2291 (76.9)	<.001
Intensity										
Take it easy	—	3390 (81.0)	267 (15.4)	—		—	6244 (88.6)	701 (31.4)	—	
Heavy breath/sweat	—	797 (19.0)	1450 (83.8)	4289 (83.6)	<.001	—	806 (11.4)	1528 (68.4)	2756 (92.5)	<.001
Near exhaustion	—	—	13 (0.8)	841 (16.4)		—	—	5 (0.2)	223 (7.5)	

\*For linear trend, regression analyses were used for continuous variables;  $\chi^2$  tests were used for proportions of categorical variables.

†Defined as systolic blood pressure  $\geq 140$  mm Hg or diastolic blood pressure  $\geq 90$  mm Hg or taking blood pressure medications.

‡Based on consumption over a 2-week period.

**Table 2** Hazard Ratios of Death from All Causes and Cardiovascular Disease by PAI

PAI	Men					Women				
	Person-Years	Deaths	Rate*	HR (95% CI)†	HR (95% CI)‡	Person-Years	Deaths	Rate*	HR (95% CI)†	HR (95% CI)‡
<b>CVD</b>										
Inactive	211,495	896	4.2	1.00 (Reference)	1.00 (Reference)	206,964	635	3.1	1.00 (Reference)	1.00 (Reference)
≤50	99,919	758	7.6	1.02 (0.93-1.13)	1.07 (0.97-1.18)	184,144	779	4.2	0.81 (0.73-0.90)	0.87 (0.78-0.96)
51-99	45,179	184	4.1	0.83 (0.71-0.97)	0.89 (0.76-1.05)	60,892	149	2.4	0.76 (0.64-0.91)	0.86 (0.72-1.03)
≥100	137,837	369	2.7	0.71 (0.63-0.80)	0.83 (0.73-0.93)	83,254	97	1.2	0.62 (0.50-0.77)	0.77 (0.62-0.96)
				<i>P</i> -trend <.001	<i>P</i> -trend <.01				<i>P</i> -trend <.001	<i>P</i> -trend <.01
<b>All-causes</b>										
Inactive	211,495	2311	10.9	1.00 (Reference)	1.00 (Reference)	206,964	1724	8.3	1.00 (Reference)	1.00 (Reference)
≤50	99,919	1755	17.6	0.94 (0.89-1.00)	0.99 (0.93-1.05)	184,144	2055	11.2	0.85 (0.79-0.90)	0.89 (0.84-0.95)
51-99	45,179	450	10.0	0.79 (0.72-0.88)	0.86 (0.77-0.95)	60,892	420	6.9	0.80 (0.72-0.90)	0.87 (0.78-0.97)
≥100	137,837	1011	7.3	0.75 (0.70-0.81)	0.87 (0.80-0.94)	83,254	336	4.0	0.72 (0.64-0.81)	0.83 (0.74-0.94)
				<i>P</i> -trend <.001	<i>P</i> -trend <.001				<i>P</i> -trend <.001	<i>P</i> -trend <.001

CI = confidence interval; CVD = cardiovascular disease; HR = hazard ratio; PAI = personalized activity intelligence.

\*Rate per 1000 person-years.

†Adjusted for age by including the attained age as the time scale.

‡Adjusted for age, smoking (smoker, nonsmoker), body mass index (underweight, normal-weight, overweight), hypertension (normal, hypertensive), alcohol consumption, and education.

≥100 PAI was associated with reduced risk of all-cause and cardiovascular disease mortality (Supplementary Table 3, available online).

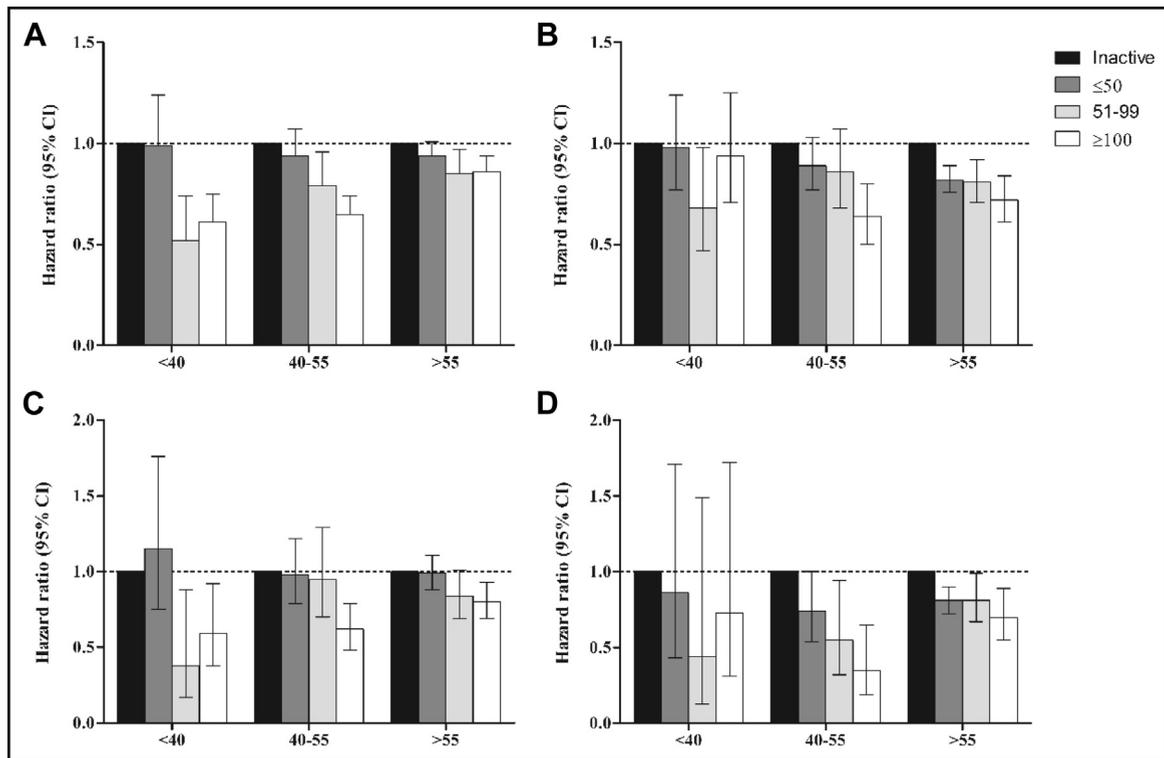
In a separate analysis, we assessed the hazard ratio for the combination of PAI and physical activity recommendations. Compared with the reference group of ≥100 PAI and meeting the recommendations, participants with ≥100 PAI and below the recommendations did not have a significantly increased risk of dying from cardiovascular disease: HR, 1.07 (95% CI, 0.87-1.31) (Table 3). The corresponding hazard ratio for all-cause mortality was 1.06 (95% CI, 0.94-1.19). In participants who met the physical activity recommendations but had <100 PAI, the hazard ratio was 1.27 (95% CI, 1.09-1.48) for cardiovascular disease mortality, and 1.13 (95% CI, 1.02-1.24) for all-cause mortality. The multi-adjusted sensitivity analyses of PAI and physical activity showed that physical activity was clearly not significant ( $\chi^2 = 0.79$ ,  $P > \chi^2 = .37$  for all-cause, and  $\chi^2 = 0.01$ ,  $P > \chi^2 = .98$  for cardiovascular disease mortality; Supplementary Table 4, available online). The results were not substantially altered when we excluded the first 3 years of follow-up (Supplementary Table 5, available online).

We observed that <100 PAI was associated with an average 4.7 (95% CI, 4.4-5.0) years of life lost compared with participants obtaining ≥100 PAI. As shown in Supplementary Figure 2 (available online), these estimates were 3.9 (95% CI, 3.6-4.2) years in women, and 6.0 (95% CI, 5.7-6.3) years in men. Also, the difference was more pronounced in middle-aged participants. For instance, ~7 years of life were lost in men aged 56-60 years with PAI below 100.

## DISCUSSION

We derived and validated a new personalized metric for physical activity tracking using large-scale data of a healthy Norwegian population, including approximately 1 million person-years of observations over more than 26 years. The main finding of the study was that obtaining ≥100 PAI significantly reduced the risk of dying prematurely from all causes and from cardiovascular disease among men and women, and in different disease subgroups. Of particular interest was the observation that obtaining a PAI level of 100 weekly gave similar reduction in risk of dying prematurely regardless of whether or not the current recommendation for physical activity was met, demonstrating that PAI may be a more relevant metric than current worldwide physical activity recommendations for determining whether an individual's activity level is sufficient to achieve substantial health benefits.<sup>8,10</sup>

The application and utility of PAI could be twofold: 1) prevention of premature cardiovascular disease and 2) promotion of physical activity. With advances in technology, which include multiple wearable devices and Web-based applications, it is now much easier to self-monitor physical activity than it was a decade ago. In PAI, one could use an algorithm integrated into a health app or



**Figure 1** Hazard ratios of death associated with personalized activity intelligence in age groups (years). (A) All-cause mortality in men; (B) all-cause mortality in women; (C) cardiovascular disease mortality in men; (D) cardiovascular disease mortality in women. CI = confidence interval.

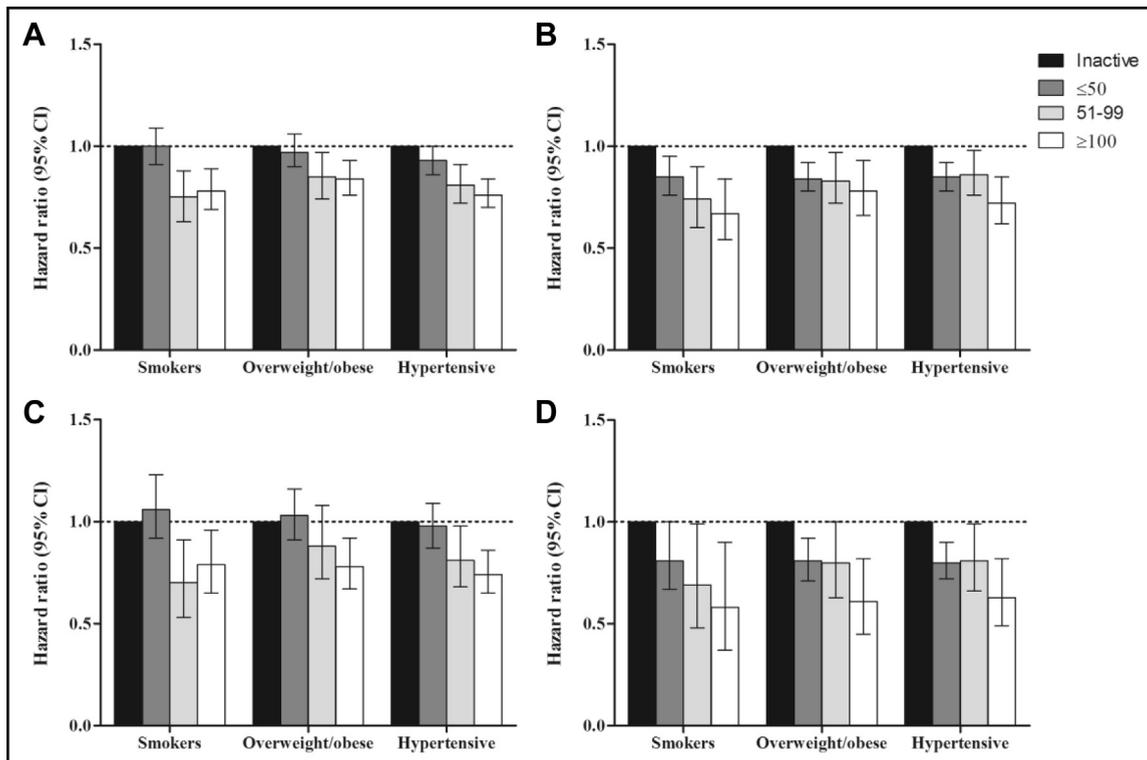
wearable device that measures heart rate continuously, and potentially made available to the general public worldwide, allowing individuals across the world to track their activity levels using a single, easily understandable metric. Not only could this allow individuals to determine if they are performing sufficient physical activity to achieve better health and longevity, but the use of PAI and readily available feedback could also motivate individuals to increase the quantity or intensity of their physical activity. Possibly, this practice could translate into prevention of premature cardiovascular disease and all-cause mortality.

The finding that it is not necessary to exercise daily to obtain substantial health benefits, as long as one obtains 100 PAI weekly, is of particular interest, and in line with previous studies reporting that fewer sessions, if performed at higher intensities, provide similar or larger health benefits compared with frequent, low-intensity activity of longer duration.<sup>12,28-30</sup> Although we acknowledge the concern that high-intensity activity may be less achievable for previously inactive people, highlighting the benefits of shorter bouts of higher intensity are important, as lack of time for physical activity/exercise is the predominant reason for the majority of people not to be physically active on most days of the week,<sup>31,32</sup> making it difficult to fulfill current physical activity recommendations. The algorithm also incorporates the fact that the major reduction in mortality occurs between the least active and the less active people, and it is easier to earn the first 50 vs the next 50 PAI. The key is to accumulate adequate

active time above the relative heart rate threshold in order to earn PAI, and the higher the intensity, the shorter the time needed to obtain 100 PAI. So far, this issue has been difficult to incorporate and promote through self-measurement devices that focus predominantly on number of steps or accumulated time in motion. In terms of risk, no further reductions in cardiovascular disease or all-cause mortality were observed for scores progressively higher than 100 PAI.

### Strengths and Limitations

The main strengths of the present study include a large population-based cohort of healthy men and women, the long-term and virtually complete follow-up, and information on various confounding factors. A limitation of the study is that physical activity data in the validation cohort was obtained only at one time-point, which is inherently prone to classification bias. However, in prospective studies, the nature of the misclassification is most likely nondifferential in relation to future disease, and therefore likely to yield underestimates of the true effects. The HUNT study population is ethnically homogenous, predominantly Caucasian, and has a better baseline health profile than many other large populations. However, similar effect of physical activity on risk reduction has been demonstrated in the HUNT population<sup>12,30</sup> and studies from around the world.<sup>9,11,28,29</sup> Also, as heart rate (resting and maximal) seems to be consistent throughout the globe, chances are strengthened that PAI is



**Figure 2** Hazard ratios of death associated with personalized activity intelligence in sub-groups. (A) All-cause mortality in men; (B) all-cause mortality in women; (C) cardiovascular disease mortality in men; (D) cardiovascular disease mortality in women. Overweight/obesity was body mass index  $\geq 25 \text{ kg} \cdot \text{m}^{-2}$ . Hypertension was defined as systolic blood pressure  $\geq 140 \text{ mm Hg}$  or diastolic blood pressure  $\geq 90 \text{ mm Hg}$  or taking blood pressure medication. CI = confidence interval.

universal across ethnicities. Nonetheless, the generalizability of the PAI algorithm in ethnically diverse populations with varying cardiovascular disease risk warrants investigation. Despite the large number of study participants, the number of deaths in certain subgroups was low, specifically the age group  $<40$  years in women. As a result, the corresponding effect estimates were not precise, and

therefore, one should be careful in drawing firm conclusions related to these subgroups. We recognize that people could have changed their activity status, and hence PAI, during the follow-up time. However, this may be a potential strength of our validation study, stressing that a single measure of PAI at baseline is associated with long-term cardiovascular disease mortality.

**Table 3** Hazard Ratio of Death According to Physical Activity Recommendations and PAI

PAI	PA Recommendations	Deaths	HR (95% CI)*	HR (95% CI)†
CVD	Yes	338	1.00 (Reference)	1.00 (Reference)
		128	1.09 (0.89-1.34)	1.07 (0.87-1.31)
	<100	331	1.46 (1.25-1.70)	1.27 (1.09-1.48)
		3070	1.43 (1.27-1.60)	1.24 (1.11-1.40)
All-causes	Yes	974	1.00	1.00
		373	1.10 (0.98-1.24)	1.06 (0.94-1.19)
	<100	771	1.28 (1.17-1.41)	1.13 (1.02-1.24)
		7944	1.30 (1.22-1.39)	1.15 (1.07-1.23)

CI = confidence interval; CVD = cardiovascular disease; HR = hazard ratio; PA = physical activity; PAI = personalized activity intelligence.

\*Adjusted for age by including the attained age as the time scale, and sex.

†Adjusted for age, sex, smoking (smoker, nonsmoker), body mass index (underweight, normal-weight, overweight), hypertension (normal, hypertensive), alcohol consumption, and education.

## Future Perspectives

The major strength of the PAI algorithm lies in its applicability when incorporated in self-monitoring devices that allow for continuous measurement of heart rate. Future studies are warranted to validate the algorithm against continuous heart rate measurements, and ultimately in long-term randomized trials to evaluate the effect on cardiorespiratory fitness, cardiovascular risk, and adherence to physical activity in diverse populations.

## CONCLUSION

PAI is associated with long-term cardiovascular disease and all-cause mortality and could be incorporated in self-measurement instruments to provide an opportunity for promotion of physical activity, as it offers individuals a variety of options and choices relating to the quantity, quality, or intensity of physical activity to achieve maximum health benefits. The use of PAI could help clinicians, healthy lifestyle industry, and worksite wellness initiatives worldwide in efforts to increase effective physical activity goals across the globe.

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**Authorship:** BMN, CRG, and JN had full access to all of the data in the study, analyzed the data, interpreted the results and wrote the paper. CJL and UW provided critical inputs and wrote the paper. All authors had access to the data and participated in writing the manuscript.

## SUPPLEMENTARY DATA

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