Association between device-measured physical activity and incident heart failure: A prospective cohort study of 94,739 UK Biobank participants

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Abstract

Background: Studies of objectively measured physical activity (PA) have investigated acute cardiovascular outcomes but not heart failure (HF), an emerging chronic condition. This study aimed to investigate the dose-relationship between device-measured PA and HF by intensity of PA.

Methods: This was a prospective cohort study of 94,739 UK Biobank participants who had device-measured PA measured in 2013-2015 and were free from myocardial infarction and heart failure. PA was measured using a wrist-worn accelerometer and time spent on light- (LPA), moderate- (MPA), and vigorous-intensity PA (VPA) were extracted. Incident HF was ascertained from linked hospital and death records. Cox proportional hazard models with cubic penalised splines were used to study the associations, adjusted for sociodemographic and lifestyle factors. Competing risk was handled using cause-specific hazard ratios (HRs).

Results: The overall incidence of HF was 98.5 per 10,000 person-years over a median 6.1 years of follow-up. Compared with participants who undertook no MVPA, those who performed 150-300 minutes of MPA/week (HR 0.37, 95% CI 0.34-0.41) and 75-150 minutes of VPA/week (HR 0.34, 95% CI 0.25-0.46) were at lower HF risk. The association between VPA and HF was reverse J-shaped with a potentially lower risk reduction above 150 minutes/week.

Conclusions: Device-measured PA, especially MPA, was associated with lower risk of HF. Current VPA recommendations should be encouraged but not increased. In contrast, increasing MPA may be beneficial even among those meeting current recommendations.

Keywords: physical activity; accelerometery; heart failure; public health

Abbreviations

BMI: body mass index
CVD: cardiovascular disease
FEV_1: forced expiratory volume in 1 second
IQR: interquartile range
HF: heart failure
HR: hazard ratio
LPA: light-intensity physical activity
METs: metabolic-equivalent of tasks
MPA: moderate-intensity physical activity
PA: physical activity
SD: standard deviation
VPA: vigorous-intensity physical activity
WHO: World Health Organization

Clinical Perspective

What is new?

- This study shows, for the first time, that objectively measured physical activity is associated with incident heart failure independent of sociodemographic, lifestyle, and clinical factors.
- The association between moderate-intensity physical activity and heart failure indicates benefit beyond the current World Health Organisation physical activity recommendations.

What are the clinical implications?

- Promoting physical activity could be beneficial in reducing the population burden of heart failure.
- Moderate-intensity physical activity should be encouraged in individuals who are at high risk of heart failure.

Introduction

Despite the declining trend in cardiovascular disease (CVD) mortality[1], CVD remains a leading contributor to the global burden of disease[2], transitioning from acute events to chronic disease including heart failure (HF).[1] Identifying modifiable lifestyle factors for HF could potentially reduce its population burden.

Physical activity (PA) is one of the modifiable risk factors shown to be strongly associated with CVD outcomes. A recent meta-analysis of 36 prospective studies of over 3 million participants reported that adhering to the WHO recommendation of 150 minutes per week of moderate-to-vigorous intensity PA (MVPA) was associated with 21% lower CVD risk.[3] However, most of the evidence available to date has been derived from self-reported PA, which is prone to recall bias and which, therefore, could obscure the true magnitude and nature of the association between PA and CVD.

Most evidence from device-measured PA focuses on acute CVD outcomes. A study of 3,343 older adults reported a 41% lower risk of MI and stroke for each 30-minute/day increment in moderate- and vigorous-intensity PA (MVPA).[4] Similarly, a recent study from the UK Biobank cohort reported that, compared to those in the lowest PA quartile, those in the highest had between 50% and 60% lower risk of ischaemic heart disease, stroke, and overall CVD.[5] However, none of these studies compared moderate PA (MPA) and vigorous PA (VPA).

In the current PA recommendations, it is assumed that the same duration of VPA could provide twice the benefits of MPA, e.g. the WHO recommended at least 150-300 minutes/week MPA or 75-150 minutes/week VPA. However, this assumption is based on experimental evidence that higher intensity exercise could elicit a larger increase in aerobic capacity in clinical studies using self-reported PA. More importantly, even though MI can lead to HF, an increasing number of HF cases occur in people who have not previously had acute CVD events.

It has been estimated that PA currently prevents 15% of premature deaths.[6] However, this figure was derived from self-reported data,[6] which is subject to reporting bias. Previous studies on all-cause mortality suggest that the relative risk estimates derived from device-based PA may be double.[7, 8]

The present study, therefore, investigated the dose-response association between device-measured PA and HF by intensity of PA. The public health implications were also explored using preventable fractions.

Methods

The UK Biobank cohort enrolled over 500,000 participants aged 37-73 years at baseline from the general population (5.5% response rate).[9] In brief, between 2006 and 2010, participants attended one of 22 assessment centres across Scotland, England and Wales.[10, 11] All participants completed a touch-screen questionnaire, had physical measurements taken, and provided blood, urine, and saliva samples at

baseline. More information about the UK Biobank protocol can be found online (https://www.ukbiobank.ac.uk/). Because of the sensitive nature of the data collected for this study, requests to access the dataset from qualified researchers may be sent to the UK Biobank at http://ukbiobank.ac.uk.

Device-measured PA

Axivity AX3 wrist-worn triaxial accelerometers were used to collect objective PA measurements from 103,686 UK Biobank participants between 2013 and 2015. Participants who provided an email address to UK Biobank were invited at random.[12] The dominant wrist of each individual was used over a period of 7 days at 100 Hz, as has been described elsewhere.[12] The 7,161 participants with insufficient wear time (<72 hours), missing data, or poor device calibration were excluded, leaving 96,525 participants with valid device-measured PA data. More details about data collection and processing can be found elsewhere.[12]

Minutes per week (min/week) of light PA (LPA), MPA and VPA were determined as the time spent in 30-125 mg, 125-400 mg, and >400 mg intensity activity, respectively.[13, 14] In addition, total PA and total MVPA was expressed as the total metabolic equivalent of tasks (METs) minutes per week, accounting for both intensity and duration.

Outcome ascertainment

Incident HF events were extracted from both hospital records and death certificates to ensure comprehensive ascertainment. Dates and causes of hospital admissions were identified via record linkage to Hospital Episode Statistics (England and Wales) and the Scottish Morbidity Record (Scotland). Details of the linkage procedure can be found at http://content.digital.nhs.uk/services. The start of follow-up was the date when all PA device measurements were completed. Participants with MI and HF prior to that date, based on both self-report at the baseline assessment and retrospective record linkage to hospital and primary care records, were excluded from the analyses (Figure S1). Hospital admission data were available until February 2021 in England and Scotland, and February 2018 in Wales. Using the International Classification of Diseases, 10th revision, HF was defined as I50, I42.0, I42.6, I42.7, I42.9, I11.0.

Covariates

Age, when PA data were collected, was determined from dates of birth and PA assessment. Ethnicity was self-reported and categorised into White, South Asian, Black, Chinese, other and mixed ethnic background. Area-based socioeconomic deprivation was derived from postcode of residence, using the Townsend score.[15] Educational attainment was based on self-report of the highest level of qualification. Smoking status was self-reported and categorised as never, former or current smoker. Alcohol consumption was calculated based on self-reported frequency and volume of drinking. Dietary intake of fruit and vegetables, red meat, processed meat, and oily fish was based on a food frequency questionnaire, self-completed at baseline. Height and body weight were measured by trained nurses during the

baseline assessment. Body mass index (BMI) was calculated as (weight in kg)/(height in m)^2. Hypertension was ascertained by either self-report of physician diagnosis, use of antihypertensive medication, or measured systolic blood pressure ≥140 mmHg. Similarly, type 2 diabetes was defined as either self-report of physician diagnosis or use of anti-diabetic medication or serum glycated haemoglobin ≥48 mmol/mol. Multimorbidity and medication use was self-reported. Forced expiratory volume in 1 second (FEV_1), as an indicator of lung function and respiratory disease, was assessed using spirometry following a standard protocol.

Statistical analyses

Descriptive characteristics by quartile of total PA in MET-minutes/week are presented as means with standard deviation (SD) for continuous variables and frequencies with percentages for categorical variables.

Nonlinear associations between PA and incident HF were investigated using penalised cubic splines fitted in Cox proportional hazard models. The penalised spline is a variation of the basis spline, which is not as sensitive to knot numbers and placements as restricted cubic splines.[16] Nonlinearity in exposure-outcome relationships was tested by likelihood ratio tests comparing models with PA splines and models with linear PA terms. The proportional hazard assumption was checked using Schoenfeld residuals. All analyses were adjusted for these confounders: age, sex, ethnic group, deprivation, education, smoking, alcohol intake, and dietary intake. Competing risk due to death from other causes was addressed using cause-specific HR where mortality was censored at date of death. Proportional hazard

assumptions were tested using the Schoenfeld residuals and revealed no violations (p-values 0.09-0.14).

Three sensitivity analyses were performed. Firstly, LPA, MPA and VPA were mutually adjusted to examine whether the associations were likely to be due time spent in other PA intensity. Secondly, adiposity (BMI and waist-hip circumference), hypertension, type 2 diabetes, and statin use at baseline were additionally adjusted as these could limit the ability of participants to perform PA. These variables were not included in the main analyses as they could also be mediators of an association between PA and HF. Thirdly, a two-year landmark analysis was conducted excluding participants who developed HF in the first two years of follow-up, in order to reduce the risk of reverse causation due to sub- or pre-clinical HF at baseline.

A separate analysis was conducted using categorised MPA and VPA variables. MPA was categorised as <149, 150-300, and >300 minutes; and VPA as: <75, 75-150, and >150 minutes. These cut-offs were chosen based on the current WHO PA recommendations (150-300 minutes MPA; 75-150 minutes VPA). LPA was not used in risk matrix and PFP because the current PA recommendations have not included LPA. A risk matrix was constructed to illustrate the joint HR for MPA and VPA categories.

Preventable fractions for the study population (PFP)[17] were calculated to estimate the proportions of all incident HF cases that could have been prevented if the individuals in specific MVPA categories were as active as the most active group, assuming that the associations were causal. All analyses were conducted using the

'survival' packages in R 4.0.2. A p-value below 0.05 was considered statistically significant.

Ethical Approval

UK Biobank was approved by the North-West Multi-Centre Research Ethics Committee (Ref: 11/NW/0382). The study protocol is available online (http://www.ukbiobank.ac.uk/). This work was conducted under the UK Biobank application number 7155.

Results

Of the 502,488 UK Biobank participants, 96,525 had valid device-measured PA data (Figure S1). Of these, 1,786 were excluded due to prevalent MI and/or HF at baseline, resulting in an effective sample size of 94,739. The median (IQR) follow-up period was 6.1 (5.5-6.6) years. The overall incidence rate of HF was 98.5 per 10,000 person-years.

Participant characteristics by total PA are shown in Table 1. Participants who undertook more PA were generally younger, more likely to be female, White, and university graduates, less likely to smoke, and consumed more fruit and vegetables and less red and processed meat. They also had lower BMI and were less likely to have hypertension and type 2 diabetes, and take statins.

Total PA, MVPA, and time spent on LPA, MPA, and VPA were all associated with lower risk of incident HF when adjusted for sociodemographic and lifestyle factors. From the analysis using penalised splines, compared with participants who took no MVPA at all, those who performed 150-300 minutes of MPA/week (cause-specific HR 0.37, 95% CI 0.34-0.41) and 75-150 minutes of VPA/week (cause-specific HR 0.34, 95% CI 0.25-0.46) were at lower HF risk (Figure 1). The lowest HF risk was achieved at 600 minutes/week MPA then plateaued thereafter. The results from two-year landmark analyses were consistent with those from the main analyses. The association between VPA and HF was reverse J-shaped and with potentially smaller reduction in risk after 150 minutes/week. The associations of total PA, LPA ad MPA were generally similar for sex-specific analysis (Figure S2), and when adiposity, FEV_1, type 2 diabetes, hypertension, statin use, and morbidity count were additionally adjusted as a sensitivity analysis. However, the association with VPA became U-shaped (Figure S3). When LPA, MPA, and VPA were mutually adjusted, LPA was associated with higher HF risk and VPA was associated with lower HF risk only when <150 minutes/week (Figure S4); the association of MPA remained unchanged.

The risk matrix illustrating the joint associations between MPA and VPA and HF is shown in Figure 2 based on HRs from Table S1. Performing more MPA, even beyond the current recommendation of 150-300 minutes/week, was associated with reductions in HF risk. Performing VPA 75-150 minutes/week was associated with lower HF risk only when individuals performed >300 minutes/week of MPA.

Table 2 shows the proportions of HF cases that could have been prevented by increased PA. Assuming the associations to be causal, which cannot be confirmed in this study, 7.19% of incident HF cases in the study population were attributed to <150 minutes/week of MPA and 23.61% to <75 minutes/week of VPA. The preventable fraction for MPA was small because only 0.68% of the study participants performed <150 minutes of MPA. Conversely, 90.18% of participants performed <75 minutes of VPA, resulting in more HF cases being preventable by increasing VPA.

Discussion

Principal findings

This study showed that higher MPA was associated with lower risk of HF across the full range of MPA, whereas there was a potentially U-shaped association between VPA and HF. The association between LPA and HF was inconsistent across analysis. Undertaking more MPA than currently recommended may produce additional benefit in reducing HF risk but it might not be the case for VPA, and indeed very high level of VPA may be less beneficial. At the population level, given that most individuals in UK Biobank performed <25 minutes of VPA/week, promoting VPA, even to the 25-50 minutes/week bracket could potentially translate to reducing the HF burden by a substantial amount. There is also potential population benefit in promoting MPA beyond its current 150-300 minutes recommendation. It is important to note that the current reported physical activity is exceptionally high compared to self-reported data but that is largely because self-reported data only account for

bouted PA (typically >10 minutes) whereas accelerometer measurement also captures unbouted PA. This highlights the importance to re-examine the current PA guidelines which are primarily based on self-reported data.

Strength and limitations

This study has several important strengths. First and foremost, it utilised device-measured PA, which should accurately reflect the actual PA level of participants and is robust against recall or reporting bias. We also examined the associations by PA intensity in relation to HF, an emerging chronic CVD. To reduce reverse causation due to sub-/pre-clinical conditions, we conducted landmark analyses, excluding participants who were diagnosed with HF within the first two years of follow-up. BMI, hypertension, type 2 diabetes, other comorbidities, FEV_1, and use of statins could be mediators or confounders and were additionally adjusted in a sensitivity analysis. These sensitivity analyses provided largely consistent results, increasing confidence in the findings. The main difference observed in the sensitivity analysis was in VPA, where the association became U-shaped. This could be related to the potential benefits of VPA mainly mediated through the reduction of these conditions (assuming these are mediators) or those conditions inhibit a very high amount of VPA (assuming these are confounders). Furthermore, this study considered the competing risk due to deaths from other causes. This is important in the analyses as individuals who are physical inactive tend to die earlier and thus have a lower chance of developing heart failure. However, this study still has several caveats. Firstly, UK Biobank is not representative of the UK population, with evidence of a healthy volunteer selection bias. Estimates of effect size were found to be consistent

with population-representative cohorts,[18] but PA levels are higher among UK Biobank participants. Therefore, the calculated PFPs are likely to be an underestimate of the contribution of PA to HF in the general population. PFPs assume that the association is causal which cannot be confirmed in an observational study. In spite of adjustment for a wide range of covariates, including obesity, multimorbidity and FEV_1, and a 2-year landmark analysis residual confounding and reverse causation cannot be ruled out in observational studies and causal interpretation should be cautioned. Nonetheless the PFPs estimated in this study could still be used to compare and triangulate with existing literature. Additionally, the time spent in sedentary behaviours and light intensity PA might not be clearly differentiated in the wrist-accelerometers. Therefore, future studies are needed to investigate whether time spent in light intensity PA could also be associated with HF risk. Lastly, there were no reliable information to further distinguish HF, into with and without preserved ejection fraction, which may have differential association with PA.

Comparison with other studies

PA is likely to be causally protective of HF based on extrapolation of randomised controlled trials of PA interventions on HF risk factors.[19-21] The underlying biological mechanisms for the association between PA and HF have not been fully elucidated but could relate to immune-inflammatory response, such as tumour necrosis factor-alpha (TNF-α).[22-24] TNF-α was found to lead to atherosclerosis and elevated blood pressure through accelerated interleukin 6 (IL-6), which acts on vascular endothelial cells.[25] The existing evidence suggests that aerobic exercise could induce significant reductions in IL-6 and TNF-α.[23] Also, higher serum cholesterol or triglycerides leads

to atherosclerosis through oxidation of lipoprotein particles by macrophage phagocytosis, which is the main cause of increased risk of HF.[26] PA could change the number and size of lipoprotein particles, accelerate the breakdown of low-density lipoproteins (LDL) and reduce their transportation of cholesterol to the arterial wall, which could all be mechanisms for lower CVD, and thus HF risk.[26] Adiposity is also a plausible mechanism linking PA and HF as evident in the current analysis adjusted for BMI and waist-hip circumference.

The limited evidence on device-measured PA and HF is generally consistent. A prospective cohort study of 1,181 older men found MVPA to be associated with lower risk of MI, stroke and HF but has not studied LPA.[27] A previous study on 93,669 UK Biobank participants showed device-measured PA was inversely associated with risk of AF (HR 0.82, 95% CI 0.75–0.89) and stroke (HR 0.76, 95% CI 0.64–0.90), however HF was not included as an outcome.[28]

Several studies have examined device-measured PA and overall CVD risk by intensity but not in HF. Contrary to our results, one study showed that VPA, but not MPA or LPA, was associated with lower risk of stroke.[29] However, the previous study was cross-sectional and utilised self-reported PA and, thus, was susceptible to reverse causation and recall bias. A previous study using UK Biobank data, found that MPA (HR 0.46, 95% CI 0.41–0.51) and VPA (HR 0.41, 95% CI 0.37–0.47) had similar magnitudes of associations in the quartile analysis.[5] However, the study did not mutually adjust MPA and VPA and, thus, the hazard ratios could not be meaningfully compared. The study also did not include emerging CVD outcomes, such as HF.

Implications

This current study, along with previous evidence of causality[19], suggests that promoting MVPA in the population could substantially reduce the burden of HF. Because the associations did not plateau until a very high level of MPA, people who already meet the current WHO recommendations could still gain benefit from increasing their PA further. The WHO recommendations are largely based on evidence from self-reported PA and should be regarded as a minimum MPA target. Future studies should consider how we can directly compare evidence derived from self-reported PA to objectively measured PA.

Promotion of VPA in the population is supported by the findings of its high PFPs. Nonetheless caution should be exercised as it only appears beneficial to promote VPA among individuals who have sufficient MPA. Its potential U-shaped association should also be noted, whereby individuals who performed over 150 minutes of VPA per week were at a similar risk of those who performed no VPA at all, and potentially higher risk than those who met the recommendations. This could be related to the VPA-associated adverse events shown in trials,[30, 31] as well as adverse heart remodelling (e.g. hypertrophic cardiomyopathy) due to prolonged exposure to vigorous exercise as seen in elite athletes.[32] A previous study also showed that excessive long-term exercise could accelerate heart failure in rats.[33] It should also be noted that PA at very high intensity could be associated with discomfort and might not be easy to adopt or maintain, particularly among those who are at a higher risk of CVD.[34, 35]

Conclusions

In conclusion, device-measured PA, especially MPA, was associated with lower risk of HF. Performing MPA beyond current recommendation is associated with further HF risk reduction. The associations of VPA should be carefully examined before considering promotion of very high levels of VPA in the general population.

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Conflict of Interest Disclosures

PW has received research grants from Roche Diagnostics, AstraZeneca and Boehringer Ingelheim outside the submitted work, and NS has received grants from AstraZeneca, Boehringer Ingelheim, and Roche Diagnostics, and personal fees from Afimmune, Amgen, AstraZeneca, Boehringer Ingelheim, Eli Lilly, Hanmi Pharmaceuticals, Merck Sharp & Dohme, Novartis, Novo Nordisk, Pfizer, and Sanofi outside the submitted work. All other authors declare no conflict of interest.

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Supplemental Materials

Figures S1-S4

Table S1

Table 1. Participant characteristics

	Device-measured Total PA, MET-minutes/week			
	Q1 (≤3856)	**Q2 (>3856-4642)**	**Q3 (>4642-5489)**	**Q4 (>5489)**
Total n	23,452	23,701	23,663	23,923
Age, years, mean (SD)	58.23 (7.52)	56.59 (7.72)	55.55 (7.75)	53.95 (7.68)
Male	12169 (51.9)	10375 (43.8)	9532 (40.3)	8716 (36.4)
Ethnic minority	710 (3.0)	759 (3.2)	801 (3.4)	989 (4.1)
Deprivation index, mean (SD)	-1.56 (2.92)	-1.76 (2.81)	-1.83 (2.75)	-1.75 (2.78)
University education	9707 (41.4)	10483 (44.2)	10470 (44.2)	10279 (43.0)
Smoking				
Never	12675 (54.0)	13730 (57.9)	13857 (58.6)	14248 (59.6)
Previous	8737 (37.3)	8449 (35.6)	8307 (35.1)	8247 (34.5)
Current	2040 (8.7)	1522 (6.4)	1499 (6.3)	1428 (6.0)
Weekly dietary intake, mean (SD)				
Alcohol, units	16.02 (17.25)	15.89 (15.96)	15.72 (15.45)	15.56 (15.49)
Fruits/vegetable, portions	3.91 (2.21)	4.15 (2.25)	4.27 (2.20)	4.51 (2.41)
Red meat, portions	2.17 (1.42)	2.06 (1.37)	2.00 (1.34)	1.95 (1.38)
Processed meat, frequency	2.91 (1.05)	2.81 (1.05)	2.77 (1.05)	2.72 (1.07)
Oily fish, frequency	2.65 (0.90)	2.67 (0.89)	2.66 (0.89)	2.64 (0.90)
BMI, kg/m^2, mean (SD)	28.34 (5.10)	26.91 (4.38)	26.21 (4.09)	25.28 (3.83)
WHR, mean (SD)	0.89 (0.09)	0.86 (0.09)	0.85 (0.08)	0.84 (0.08)
FEV1, L, mean (SD)	2.86 (0.67)	2.89 (0.68)	2.90 (0.67)	2.91 (0.66)
Number of morbidities				
0	7055 (30.1)	8919 (37.6)	9966 (42.1)	11076 (46.3)
1	7716 (32.9)	8016 (33.8)	8046 (34.0)	7917 (33.1)
2	4888 (20.8)	4321 (18.2)	3733 (15.8)	3415 (14.3)
3	2390 (10.2)	1613 (6.8)	1325 (5.6)	1093 (4.6)
4	907 (3.9)	590 (2.5)	430 (1.8)	298 (1.2)
≥5	496 (2.1)	242 (1.0)	163 (0.7)	124 (0.5)
Hypertension	13489 (57.5)	11579 (48.9)	10316 (43.6)	9152 (38.3)
Type 2 diabetes	1660 (7.1)	764 (3.2)	563 (2.4)	397 (1.7)
Statin use	4934 (21.0)	3310 (14.0)	2563 (10.8)	1749 (7.3)

MET: metabolic equivalent of task; BMI: body mass index; WHR: waist-hip ratio; PA: PA

Table 2. Preventable fraction of incident HF for the study population

	Prevalence in study sample (%)	Cause-specific HR (95% CI)	Preventable Fractions for the Population [a]	
			% (95% CI)	Cumulative % (95% CI)
MPA, min/week				
0 to <150	0.68	1 (Reference)	7.19 (6.31-8.01)	7.19 (6.30-7.96)
150 to <300	4.15	0.54 (0.46-0.64)	12.10 (9.54-14.51)	19.29 (16.83-21.87)
300 to <600	30.16	0.36 (0.30-0.43)	10.99 (5.17-17.27)	30.27 (25.52-35.96)
≥600	65.01	0.28 (0.22-0.35)	Reference	Reference
VPA, min/week				
0 to <25	60.38	1 (Reference)	20.08 (10.01-33.96)	20.08 (10.29-34.50)
25 to <50	18.52	0.83 (0.69-0.99)	2.52 (-2.07-7.24)	22.60 (12.68-36.08)
50 to <75	11.28	0.78 (0.61-1.01)	1.01 (-2.02-3.94)	23.61 (13.39-37.40)
≥75	9.82	0.70 (0.51-0.95)	Reference	Reference

MPA and VPA were modelled as categorical variables and were mutually adjusted; all adjusted for age, sex, ethnicity, education, deprivation index, smoking, alcohol intake, dietary intake of fruits/vegetables, red meat, processed meat, and oily fish.
HR: hazard ratio; MPA: moderate intensity PA; VPA; vigorous intensity PA
[a] Preventable fractions estimated the fractions of all incident HF in the study population that could have been prevented if the individuals in those PA categories were as active as the reference group

Figure 1. Association between device-measured PA and incident HF

All adjusted for age, sex, ethnicity, education, deprivation index, smoking, dietary intake of alcohol, fruits/vegetables, red meat, processed meat, and oily fish. Adiposity (body mass index and waist hip circumference) was additional adjusted in the results shown in the second row. Participants with incident HF in the first two years of follow-up were excluded in the results shown in the third row. Vertical dashed lines represent current WHO recommendations.
MET: metabolic equivalent of task; MVPA: moderate-to-vigorous intensity PA; LPA: light intensity PA; MPA: moderate intensity PA; VPA; vigorous intensity PA.

Figure 2. Risk matrix for the joint association of MPA and VPA with incident HF

Estimated in Cox regression adjusted for age, sex, ethnicity, education, deprivation index, smoking, alcohol intake, dietary intake of fruits/vegetables, red meat, processed meat, and oily fish.
Numbers presented are the associated reduction in hazard (%) compared with the least active group. There were not sufficient number of participants to estimate HRs in the blanked cells. Precision estimates are shown in Table S1.

SUPPLEMENTAL MATERIAL

Association between device-measured physical activity and incident heart failure: A prospective cohort study of 94,739 UK Biobank participants

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Figure S1. Participant flowchart

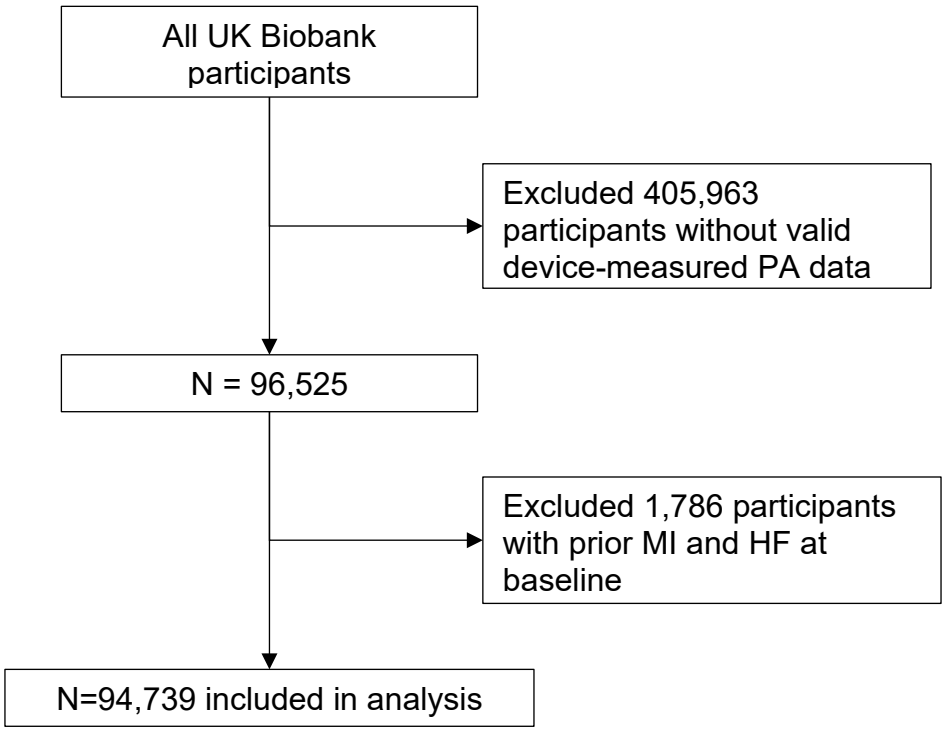
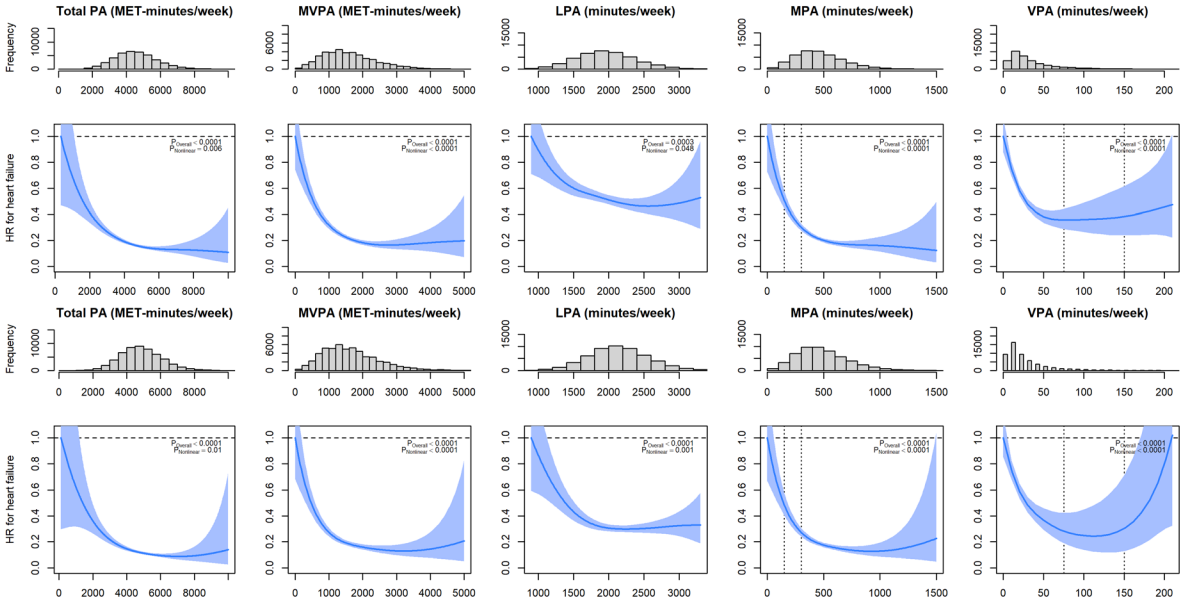
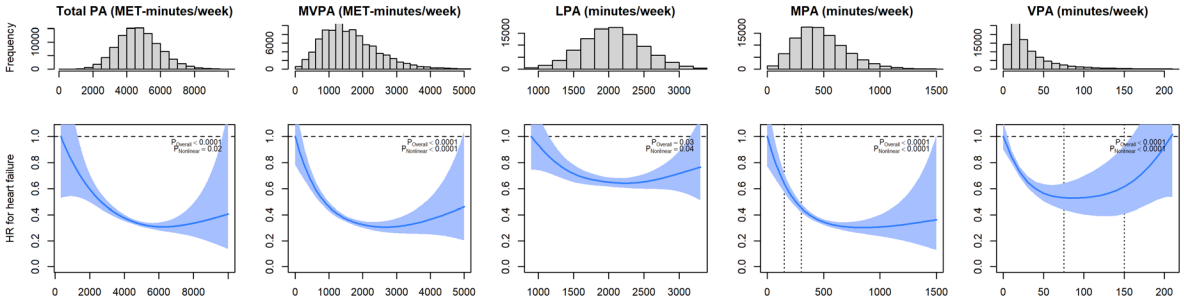


Figure S2. Association between intensity-specific PA and incident HF by sex



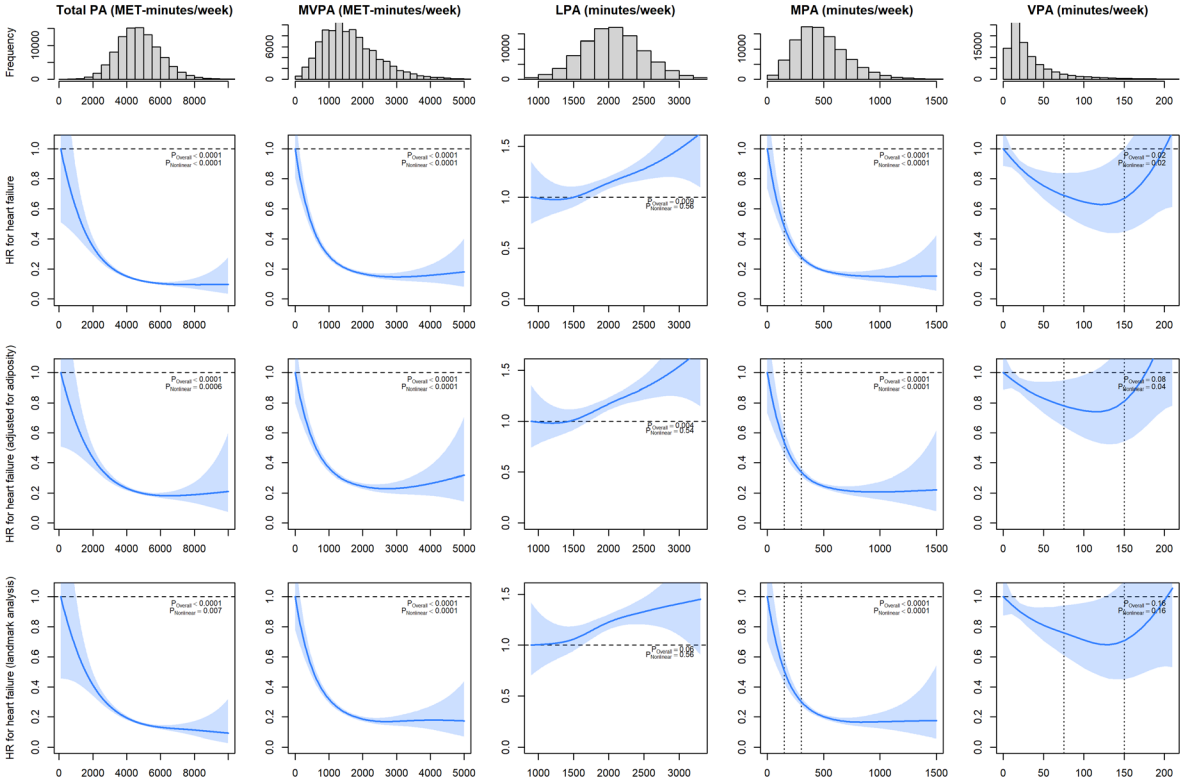
All adjusted for age, ethnicity, education, deprivation index, smoking, dietary intake of alcohol, fruits/vegetables, red meat, processed meat, and oily fish.
Vertical dashed lines represent current WHO recommendations.
MET: metabolic equivalent of task; MVPA: moderate-to-vigorous intensity PA; MPA: moderate intensity PA; VPA; vigorous intensity PA.

Figure S3. Independent association between intensity-specific PA and incident HF with additional adjusted covariates



All adjusted for age, sex, ethnicity, education, deprivation index, smoking, dietary intake of alcohol, fruits/vegetables, red meat, processed meat, and oily fish, body mass index, waist-hip circumference, FEV_1, treated and untreated hypertension and type 2 diabetes, statin use, and multimorbidity account of 43 chronic conditions.
Vertical dashed lines represent current WHO recommendations.
MET: metabolic equivalent of task; MVPA: moderate-to-vigorous intensity PA; MPA: moderate intensity PA; VPA; vigorous intensity PA.

Figure S4. Association between device-measured PA and incident HF with mutual adjustment



LPA, MPA, and VPA were mutually adjusted. All adjusted for age, sex, ethnicity, education, deprivation index, smoking, dietary intake of alcohol, fruits/vegetables, red meat, processed meat, and oily fish. Adiposity (body mass index and waist hip circumference) was additional adjusted in the results shown in the second row. Participants with incident HF in the first two years of follow-up were excluded in the results shown in the third row.
Vertical dashed lines represent current WHO recommendations.
MET: metabolic equivalent of task; MVPA: moderate-to-vigorous intensity PA; MPA: moderate intensity PA; VPA; vigorous intensity PA.

Table S1. Association between device-measured PA and incident HF for the risk matrix

	VPA, min/week		
	25 to <50	50 to <75	≥75
MPA, min/week			
150 to <300	Reference	-*	-*
300 to <600	0.59 (0.49-0.71)	0.55 (0.18-1.74)	-*
≥600	0.34 (0.28-0.40)	0.21 (0.14-0.32)	0.33 (0.19-0.58)

Data shown are HR (95% CI)

* There were not enough participants in these categories for analysis