# Joint associations of device-measured physical activity and abdominal obesity with incident cardiovascular disease: a prospective cohort study

Miguel Adriano Sanchez-Lastra [1,2,3], Ding Ding [4,5], Borja Del Pozo Cruz [6,7,8], Knut Eirik Dalene,[9] Carlos Ayán,[2,3] Ulf Ekelund,[1,9] Jakob Tarp [10]

► Additional supplemental material is published online only. To view, please visit the journal online (http://dx.doi.org/10.1136/bjsports-2023-107252).

For numbered affiliations see end of article.

**Correspondence to**
Dr Miguel Adriano Sanchez-Lastra, Department of Special Didactics, University of Vigo Education Sciences and Sports Faculty, Pontevedra 36005, Spain; misanchez@uvigo.gal

UE and JT are joint senior authors.

Accepted 9 October 2023

## ABSTRACT

**Objective** To examine the joint associations between physical activity and abdominal obesity with the risk of cardiovascular disease (CVD) events.

**Methods** We included 70 830 UK Biobank participants (mean age±SD=61.6 ± 7.9 years; 56.4% women) with physical activity measured by wrist-worn accelerometers and without major chronic diseases. Participants were jointly categorised into six groups based on their physical activity level (tertiles of total volume and specific intensity levels) and presence or absence of abdominal obesity based on measured waist circumference. Associations with incident CVD (fatal and non-fatal events) were determined using proportional subdistribution hazard models with multivariable adjustment.

**Results** After excluding events during the first 2 years of follow-up, participants were followed for a median of 6.8 years, during which 2795 CVD events were recorded. Compared with the low abdominal adiposity and highest tertile of physical activity, abdominal obesity was associated with higher risk of incident CVD, especially in those with low levels of vigorous-intensity physical activity (HR 1.42, 95% CI 1.22 to 1.64). Approximately 500 min per week of moderate-to-vigorous intensity and approximately 30–35 min of vigorous-intensity physical activity offset the association of abdominal obesity and the risk of having a CVD event.

**Conclusion** Physical activity equivalent to approximately 30–35 min of vigorous intensity per week appears to offset the association between abdominal obesity and incident CVD. About 15 times more physical activity of at least moderate intensity is needed to achieve similar results.

### WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Abdominal obesity is associated with a higher risk of developing and dying from cardiovascular disease (CVD). Whether physical activity can reduce or fully offset this association is unclear.

### WHAT THIS STUDY ADDS

⇒ We found that approximately 500 min of moderate-to-vigorous intensity physical activity or 30–35 min of vigorous-intensity physical activity per week, measured by wrist-worn accelerometers, fully offset the association of abdominal obesity with incident CVD.

### HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Encouraging people to participate in vigorous-intensity physical activity (eg, climbing stairs at a fast pace) for short periods on most days of the week appears to be a promising strategy to counteract the effects of abdominal obesity on CVD outcomes in middle-aged adults.

## INTRODUCTION

Cardiovascular diseases (CVDs) are the leading causes of deaths globally but are to a large degree preventable through modifiable risk factors such as smoking, alcohol consumption, poor diets, obesity and physical inactivity.[1]

Obesity is associated with higher risk of CVD, however, susceptibility to obesity-related CVD depends largely on body fat distribution.[2] Further, individuals with higher abdominal adiposity (ie, abdominal obesity) are at higher risk of CVD morbidity and mortality independently of total adiposity.[2–4] This association is largely mediated by impaired glucose and lipid metabolisms, which are often seen with increasing ectopic fat deposition.[5 6] Lifestyle behaviours, such as physical activity, reduce the risk of CVD via the same metabolic pathways.[7] It is, therefore, plausible that higher levels of physical activity may counteract the deleterious association between abdominal adiposity and CVD.

Accelerometer-measured physical activity captures sporadic and incidental periods of physical activity, which cannot be measured by self-report instruments.[8] It provides valid information on light-intensity physical activity (LPA) which may be beneficial for cardiometabolic health and longevity.[9] At the other end of the intensity spectrum, recent research suggests vigorous-intensity physical activity (VPA) is particularly relevant for reducing the risk for incident CVD.[10 11] However, whether different intensities of physical activity modify the association between abdominal and total adiposity and the risk for incident CVD remains unclear.

Using accelerometer-measured physical activity in a large prospective cohort of adults from the UK, we aimed to examine the joint and stratified association between abdominal adiposity and different intensities of physical activity with incident CVD. As a secondary aim, we repeated the analysis replacing abdominal adiposity with total adiposity.

Check for updates



**To cite:** Sanchez-Lastra MA, Ding D, Del Pozo Cruz B, *et al*. *Br J Sports Med* Epub ahead of print: [*please include* Day Month Year]. doi:10.1136/bjsports-2023-107252

## METHODS

This study followed the Strengthening the Reporting of Observational Studies in Epidemiology reporting guidelines (online supplemental table 1). The statistical analysis and presentation is consistent with the CHecklist for statistical Assessment of Medical Papers statement.[12]

### Data source and study population

We used data from the UK Biobank (application number 29717), a cohort of more than 500 000 participants (5.5% response rate), aged 37–73 years, recruited across the UK, who provided written informed consent. Baseline data collection, conducted between 2006 and 2010 acros 22 assessment centres, included questionnaires, physical measurements and biological sampling, and were linked to electronic registries. Between 2013 and 2015, physical activity was measured by accelerometers in a subsample of participants (n=103 613).[13]

### Exposures

#### Adiposity

Trained clinical staff performed all anthropometric measurements at baseline following standardised protocols.[13] We determined abdominal adiposity using two proxies. First, we classified participants as having abdominal obesity based on the WHO's waist circumference (WC) cut-offs (≥88 cm for women and ≥102 cm for men).[14] Second, to account for the high correlation between WC and the body mass index (BMI, weight(kg)/height (m$^2$)),[6] we derived a measure of abdominal adiposity that is statistically independent of total adiposity (BMI) by regressing WC on BMI. Using the residuals from this regression, we categorised participants into low, medium and high 'WC-for-BMI' groups, mirroring the sex-specific distribution of normal weight, overweight and obesity based on BMI.[15] Finally, we used the BMI as a proxy of total adiposity. Additional descriptive information on the creation of these measures of adiposity is included in online supplemental table 2.

#### Physical activity

Participants wore an Axivity AX3 accelerometer (Axivity, York, UK) on their dominant wrist for 24 hours during seven consecutive days. Data were collected at a sampling rate of 100 Hz and a dynamic range of ±8 g. Individual participant data were extracted from 5 s epoch time series. Exclusions criteria included <72 hours of wear time, missing data in the included 1-hour periods, implausible acceleration values (average vector magnitude acceleration >100 m*g*) or uncalibrated data.[16] Total physical activity was extracted from measured average vector magnitude in m*g*. Time spent in LPA and moderate-to-vigorous physical activity (MVPA) was determined through a machine-learning approach.[16,17] The validation sample for this approach had insufficient VPA for the algorithm to identify a useful characterisation pattern. Therefore, time spent in VPA was estimated from the average proportion of time spent in accelerations above 400 m*g*.[18] Participants were categorised into tertiles (low, medium, high) for each activity measure (further details in online supplemental table 2).

### Incident CVD

We defined incident CVD events as the first non-fatal cardiovascular event (International Statistical Classification of Diseases and Related health Problems 10th edition (ICD-10) codes I20–I25, I50 and I60–I64) from hospital inpatient records, primary or secondary diagnoses, in addition to death by cardiovascular event (primary) (ICD-10 codes I00–I99),[19] obtained from national registries. Events occurring after finishing the accelerometer measurement were considered incident. Participants were followed to incident CVD, death, withdrawal from the study, or 30 September 2021 for England, 31 July 2021 for Scotland or 31 March 2016 for Wales, whichever occurred first.

### Covariates

We identified confounders a priori based on a directed acyclic graph.[20] Detailed information on covariates is shown in online supplemental table 2. Self-reported sociodemographic covariates included ethnicity, education, living with partner and employment status. The Townsend Index was used as a marker of area-level socioeconomic status.[21] Self-reported lifestyle covariates included a dietary quality index, alcohol intake and smoking history. History of depression, hypertension and statins medication were derived from a combination of questionnaire data and verbal interview. To identify undiagnosed hypertensive patients, clinical blood pressure measurements were considered alongside self-reported data. Type 2 diabetes cases were identified using a previously developed algorithm.[22]

### Analytical sample

To reduce the risk of reverse causality, participants with major chronic diseases at baseline (eg, neurodegenerative, immunological or systemic diseases), underweight (BMI <18.5 kg/m$^2$), unable to walk, with mobility limitations or with a history of cancer or CVD before the accelerometer assessment were excluded (online supplemental table 2). Following these criteria, a total of 22 451 participants were excluded (online supplemental figure 2). Of the remaining participants, 68 090 had complete data on exposures, outcomes and covariates. We retrieved missing data on covariates for an additional 2740 participants by performing multiple imputation using chained equations with 20 datasets generated.

### Statistical analyses

Descriptive statistics included mean and SD for normally distributed continuous variables, median and range for skewed continuous variables, and percentages for categorical data.

First, we examined the independent associations of abdominal obesity and physical activity with incident CVD using the lowest WC and highest physical activity groups as the reference, respectively. Then we examined the joint associations of abdominal obesity (two categories based on WHO cut-off points and three based on 'WC-for-BMI' residuals) and physical activity tertiles (resulting in six and nine distinct categories, respectively), with incident CVD. The group with the lowest level of adiposity and highest level of physical activity was used as the reference. In addition, we examined the joint associations between total adiposity (three categories of BMI) and physical activity (resulting in nine BMI-physical activity categories) with incident CVD.

Subdistribution HRs with 95% CIs for incident CVD were calculated using Fine-Gray models to account for non-CVD deaths as a competing event. Models were left-truncated to start the follow-up time 2 years after the accelerometer assessments (2013–2015). Age was used as the underlying timescale, and models were adjusted for covariates at baseline (2006–2010), sequentially. We employed models 1, 1b and 1c for independent associations analyses, while models 1–3 were used for joint and stratified associations analyses. Model 1 was adjusted for age at accelerometer assessment (as timescale) and sex. Models 1b and

Table 1 Descriptive characteristics of the included participants by sex and group of waist circumference

| | Women (n=39 963) | | Men (n=30 867) | |
|---|---|---|---|---|
| | Low waist circumference | Abdominal obesity | Low waist circumference | Abdominal obesity |
| Age at accelerometer assessment (mean (SD)) | 60.9 (7.8) | 62.2 (7.5) | 61.7 (8.1) | 62.9 (7.6) |
| Physical activity (median, (range)) | | | | |
| Total volume (average acceleration, m*g*) | 29.1 (7.7–97.1) | 25.6 (5.9–67.5) | 28.1 (8.2–97.2) | 24.4 (5.9–89.5) |
| LPA (min/week) | 2287.3 (28.0–5799.5) | 2130.1 (47.0–5702.6) | 1910.7 (68.0–5409.5) | 1773.8 (143.6–4855.9) |
| MVPA (min/week) | 233.0 (0.0–2509.2) | 148.0 (0.0–2229.2) | 332.0 (0.0–2999.7) | 226.0 (0.0–2388.3) |
| VPA (min/week) | 6.0 (0.0–734.2) | 2.5 (0.0–468.5) | 10.5 (0.0–756.7) | 4.5 (0.0–480.0) |
| BMI categories (n; %) | | | | |
| Normal weight (18.5–24.9 $kg/m^2$) | 18 864; 65.3 | 447; 4.0 | 9656; 40.8 | 24; 0.3 |
| Overweight (25–29.9 $kg/m^2$) | 9402; 32.6 | 4674; 42.1 | 12 929; 54.6 | 2458; 34.2 |
| Obese (≥30.0 $kg/m^2$) | 603; 2.1 | 5973; 53.8 | 1089; 4.6 | 4711; 65.5 |
| Ethnicity (n; %) | | | | |
| White | 27 876; 96.8 | 10 630; 96.2 | 22 832; 96.8 | 6984; 97.5 |
| Asian | 334; 1.2 | 96; 0.9 | 341; 1.4 | 68; 0.9 |
| Black | 218; 0.8 | 178; 1.6 | 198; 0.8 | 53; 0.7 |
| Others/mixed | 365; 1.3 | 151; 1.4 | 225; 1.0 | 60; 0.8 |
| Townsend Index (mean (SD)) | −1.8 (2.8) | −1.5 (2.9) | −1.9 (2.8) | −1.7 (2.8) |
| Education (n; %) | | | | |
| No qualifications | 1851; 6.5 | 963; 8.8 | 1527; 6.5 | 669; 9.4 |
| Not college/university degree | 13 714; 47.9 | 5842; 53.2 | 10 276; 43.8 | 3676; 51.7 |
| College/university degree | 13 036; 45.6 | 4172; 38.0 | 11 655; 49.7 | 2764; 38.9 |
| Living with partner (n; %) | 21 461; 74.5 | 7801; 70.5 | 19 338; 81.9 | 5790; 80.7 |
| Employment status (n; %) | | | | |
| Unemployed (not in employment) | 2122; 7.4 | 724; 6.6 | 675; 2.9 | 244; 3.4 |
| Employed | 18 793; 65.6 | 6839; 62.0 | 16 333; 69.4 | 4778; 66.8 |
| Retired | 7737; 27.0 | 3467; 31.4 | 6526; 27.7 | 2133; 29.8 |
| Diet pattern (n; %) | | | | |
| Not meeting any targets | 3509; 12.3 | 1619; 14.9 | 5369; 23.1 | 1939; 27.6 |
| Meeting one target | 10 957; 38.5 | 4377; 40.2 | 9729; 41.9 | 3006; 42.9 |
| Meeting 2–3 targets | 13 994; 49.2 | 4883; 44.9 | 8147; 35.0 | 2069; 29.5 |
| Alcohol consumption (n; %) | | | | |
| Never | 948; 3.3 | 434; 3.9 | 402; 1.7 | 127; 1.8 |
| Former | 618; 2.1 | 285; 2.6 | 532; 2.2 | 147; 2.0 |
| Current, <3 times/week | 13 834; 48.0 | 6195; 55.9 | 8886; 37.6 | 2946; 41.0 |
| Current, ≥3 times/week | 13 443; 46.6 | 4168; 37.6 | 13 837; 58.5 | 3967; 55.2 |
| Smoking status (n; %) | | | | |
| Never | 18 492; 64.2 | 6510; 58.9 | 13 627; 57.7 | 3306; 46.1 |
| Previous | 8862; 30.8 | 3880; 35.1 | 8201; 34.7 | 3295; 45.9 |
| Current | 1450; 5.0 | 669; 6.0 | 1789; 7.6 | 572; 8.0 |
| History of depression (n; %) | 1252; 4.3 | 755; 6.8 | 648; 2.7 | 284; 3.9 |
| Type 2 diabetes (n; %) | 208; 0.7 | 481; 4.3 | 583; 2.5 | 673; 9.4 |
| Hypertension (n; %) | 10 214; 35.4 | 6361; 57.3 | 12 020; 50.8 | 5181; 72.0 |
| Statin user (n; %) | 1406; 4.9 | 1253; 11.3 | 2659; 11.2 | 1584; 22.0 |

Abdominal obesity was defined based on the WHO's cut-offs as ≥88 cm for women and ≥102 cm for men. Number varies from 68 090 (healthy diet pattern) to 70 830 because of missing data.
BMI, body mass index; LPA, light-intensity physical activity; MVPA, Moderate-to vigorous-intensity physical activity; VPA, vigorous-intensity physical activity.

2 were adjusted as model 1 plus ethnicity, education, living with partner, employment, Townsend Index, diet quality, alcohol intake, smoking and depression. Models 1b for WC and BMI exposures were also adjusted for MVPA. Models 1b and 2 were adjusted as model 1 plus ethnicity, education, living with partner, employment, Townsend Index, diet quality, alcohol intake, smoking and depression. Model 1b for WC and BMI exposures was also adjusted for MVPA. Models 1b and 2 for WC based on WHO cut-offs were additionally adjusted for BMI in continuous form.[6] We considered model 2 as the main model. Prevalent type 2 diabetes, hypertension and use of statins medication were considered mediators in the causal pathway from abdominal obesity and/or physical activity to CVD and we did not adjust for them in the main model. However, these could be conceptually considered as confounders or mediators. To address this, we created models 1c and 3, which were adjusted as models 1b and 2, respectively, but included type 2 diabetes, hypertension and statins medication as confounders in an alternative scenario (online supplemental figure 1). Proportional hazards assumption was verified using log-log plots, and interactions between adiposity and physical activity variables were assessed through likelihood-ratio tests.

**Table 2** Independent associations between physical activity, adiposity categories and risk of incident cardiovascular disease

| | n participants | n events | HRs (95% CI) Model 1 | Model 1b | Model 1c |
|---|---|---|---|---|---|
| Adiposity measures | | | | | |
| Waist circumference categories (clinical cut-off) | | | | | |
| Low (<88 cm in women, <102 cm in men) | 52 543 | 1819 | 1 (reference) | 1 (reference) | 1 (reference) |
| High (≥88 cm in women, ≥102 cm in men) | 18 287 | 976 | 1.51 (1.40 to 1.63) | 1.13 (1.01 to 1.26) | 1.11 (0.99 to 1.23) |
| Waist circumference for body mass index (BMI) residuals* | | | | | |
| Low | 28 993 | 894 | 1 (reference) | 1 (reference) | 1 (reference) |
| Medium | 29 486 | 1261 | 1.06 (0.97 to 1.16) | 1.05 (0.96 to 1.15) | 1.03 (0.95 to 1.13) |
| High | 12 351 | 640 | 1.21 (1.09 to 1.34) | 1.16 (1.04 to 1.29) | 1.13 (1.01 to 1.25) |
| BMI, categories | | | | | |
| Normal weight (18.5–24.9 kg/m$^2$) | 28 991 | 824 | 1 (reference) | 1 (reference) | 1 (reference) |
| Overweight (25–29.9 kg/m$^2$) | 29 463 | 1275 | 1.25 (1.15 to 1.37) | 1.20 (1.09 to 1.31) | 1.12 (1.02 to 1.23) |
| Obese (≥30.0 kg/m$^2$) | 12 376 | 696 | 1.79 (1.62 to 1.98) | 1.60 (1.43 to 1.77) | 1.37 (1.23 to 1.53) |
| Physical activity measures | | | | | |
| Total physical activity tertiles of m*g* (median, range) | | | | | |
| High (35.9, 31.0–97.2) | 23 586 | 660 | 1 (reference) | 1 (reference) | 1 (reference) |
| Medium (27.7, 24.7–31.0) | 23 622 | 851 | 1.07 (0.97 to 1.19) | 1.02 (0.92 to 1.13) | 1.01 (0.91 to 1.12) |
| Low (21.4, 5.9–24.7) | 23 622 | 1284 | 1.33 (1.21 to 1.47) | 1.16 (1.05 to 1.29) | 1.13 (1.02 to 1.25) |
| Light-intensity physical activity tertiles of min/week (median, range) | | | | | |
| High (2794.3, 2390.4–5799.5) | 23 605 | 790 | 1 (reference) | 1 (reference) | 1 (reference) |
| Medium (2089.1, 1808.1–2390.3) | 23 615 | 916 | 1.03 (0.93 to 1.13) | 1.01 (0.91 to 1.10) | 1.00 (0.91 to 1.10) |
| Low (1489.0, 28.0–1808.0) | 23 610 | 1089 | 1.11 (1.01 to 1.22) | 1.04 (0.95 to 1.15) | 1.03 (0.95 to 1.13) |
| MVPA tertiles of min/week (median, range) | | | | | |
| High (511.9, 349.2–2999.7) | 23 579 | 825 | 1 (reference) | 1 (reference) | 1 (reference) |
| Medium (247.1, 164.1–349.1) | 23 628 | 894 | 1.17 (1.06 to 1.28) | 1.11 (1.01 to 1.22) | 1.09 (0.99 to 1.20) |
| Low (87.5, 0.0–164.0) | 23 623 | 1076 | 1.43 (1.31 to 1.57) | 1.23 (1.12 to 1.36) | 1.20 (1.09 to 1.32) |
| Vigorous-intensity physical activity tertiles of min/week (median, range) | | | | | |
| High (31.7, 13.1–756.7) | 23 369 | 680 | 1 (reference) | 1 (reference) | 1 (reference) |
| Medium (6.1, 2.8–13.0) | 23 827 | 914 | 1.14 (1.03 to 1.26) | 1.08 (0.97 to 1.19) | 1.06 (0.96 to 1.17) |
| Low (1.0, 0.0–2.7) | 23 634 | 1201 | 1.42 (1.29 to 1.57) | 1.25 (1.13 to 1.39) | 1.21 (1.10 to 1.34) |

Model 1 was adjusted for age (used as timescale in the model) and sex. Model 1b was adjusted as Model 1 plus ethnicity, education, living with partner, employment, Townsend Index, diet quality, alcohol intake, smoking, depression. Waist circumference and BMI models were adjusted for MVPA. Waist circumference was adjusted for BMI (continuous). Model 1c was adjusted as model 1b plus type 2 diabetes, hypertension and statins medication.
*We regressed waist circumference on BMI and used the residuals to create an index of central adiposity independent of total adiposity. Residuals were used to categorise the participants as having low, medium and high waist circumference-for-BMI based on the sex-specific distribution of normal weight, overweight and obese BMI categories.
MVPA, Moderate-to vigorous-intensity physical activity.

Several supporting and sensitivity analyses were performed. First, we examined the associations between abdominal obesity and incident CVD stratified by tertiles of physical activity. Second, we repeated the joint associations analysis between abdominal obesity, physical activity and CVD stratified by sex. Third, we repeated the analysis based on WHO cut-offs without adjustment for the BMI. Finally, we also repeated the primary analysis left-truncating the models to exclude the first 5 years of follow-up. The analyses were performed using Stata V.17 statistical software (StataCorp).

## Patient and public involvement

There was no patient or public involvement in the planning, conceptualisation, research design, analysis, interpretation or composition of the findings. Results will be disseminated via institutional websites, press releases and the UK Biobank participant resource.

## Equity, diversity and inclusion statement

Our research team comprises six men and one woman from various countries in Europe and Australia. The study population is diverse in terms of age, gender, demographics and comorbidities. However, the predominantly white composition of the cohort resulted in underrepresentation of other ethnic groups. Individuals from lower socioeconomic backgrounds and marginalised communities may also have lower representation. Methodological constraints required excluding individuals with specific comorbidities and mobility limitations from analyses.

## RESULTS

We included 70 830 participants (56% women) with a mean (SD) age at the time of accelerometer assessment of 61.6 (7.9) years. Median follow-up time was 6.8 years during which 2795 CVD events occurred (2558 non-fatal and 237 fatal). Descriptive characteristics of the participants across WC categories are provided in table 1. Online supplemental table 3 presents a summary of the weekly physical activity levels (median and range) per activity tertiles and WC categories.

Abdominal obesity and low physical activity were independently associated with higher risk of incident CVD. Adjusting for BMI, abdominal obesity was associated with a 13% higher risk of CVD (HR 1.13, 95% CI 1.01 to 1.26). The HRs (95% CI) for high versus low physical activity ranged from 1.04 (0.95 to 1.15) for LPA to 1.25 (1.13 to 1.39) for VPA (table 2).

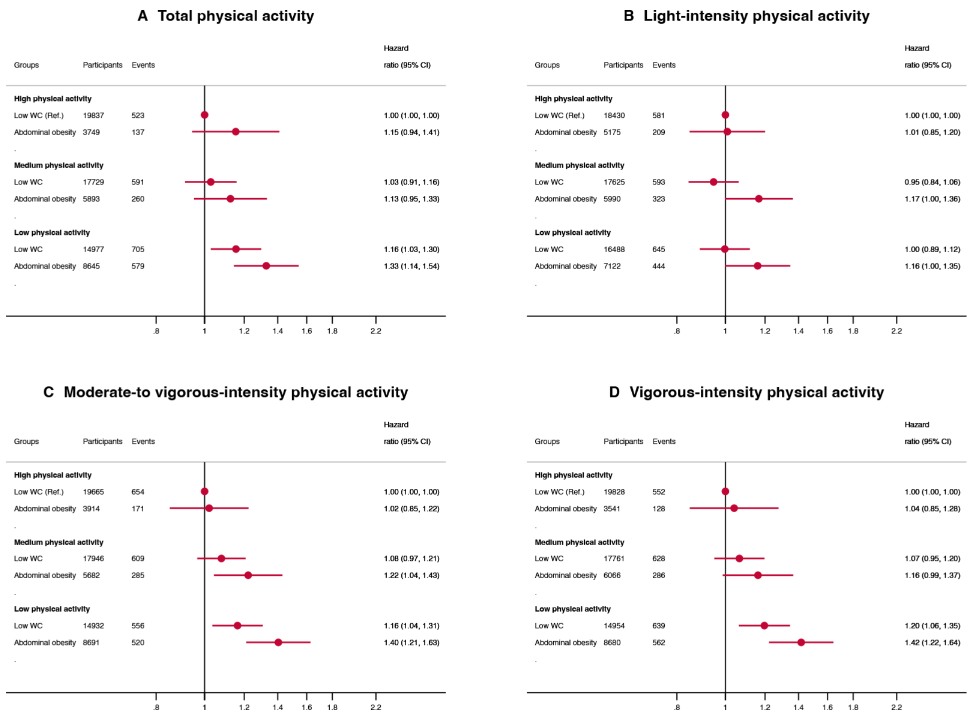



**Figure 1** Joint associations between waist circumference (WC) categories from clinical cut-offs, physical activity tertiles and incident cardiovascular disease. Ref: reference. Figure shows weekly volumes of (A) total physical activity, (B) light-intensity, (C) moderate-to-vigorous intensity and (D) vigorous-intensity physical activity. Median (range) of physical activity levels for high, medium and low tertiles were, for total physical activity, 35.9 (31.0–97.2), 27.7 (24.7–31.0) and 21.4 (5.9–24.7) m*g*, respectively. For light-intensity min/week, 2794.3 (2390.4–5799.5), 2089.1 (1808.1–2390.3) and 1489.0 (28.0–1808.0). For moderate-to-vigorous intensity min/week, 511.9 (349.2–2999.7), 247.1 (164.1–349.1) and 87.5 (0.0–164.0). For vigorous-intensity min/week, 31.7 (13.1–756.7), 6.1 (2.8–13.0) and 1.0 (0.0–2.7). Results are from main model, adjusted for age (as timescale), sex, body mass index, ethnicity, education, living with partner, employment, Townsend Index, diet quality, alcohol intake, smoking and depression.

## Joint associations between abdominal adiposity and physical activity with CVD

The highest risk of incident CVD was consistently observed in those with abdominal obesity and low physical activity, with HRs (95% CI) of 1.33 (1.14 to 1.54) for abdominal obesity and low total activity and 1.42 (1.22 to 1.64) for abdominal obesity and low VPA (figure 1). In contrast, high LPA (median=2090 min/week), high MVPA (median=512 min/week) and high VPA (median=32 min/week) mitigated the association between abdominal obesity and CVD (HRs (95% CI): 1.01 (0.85 to 1.20), 1.02 (0.85 to 1.22) and 1.04 (0.85 to 1.28), respectively). A high level of total physical activity did not completely offset the association with abdominal obesity.

The magnitude of the associations diminished after adjustment for type 2 diabetes, hypertension and statins medication as potential mediators, but the association pattern was unchanged (online supplemental figure 3).

Analysis of joint physical activity and WC-for-BMI categories supported the findings based on WHO cut-off points (figure 2). The highest risk was observed in the group with high WC and low MVPA (HR 1.64; 95% CI 1.39 to 1.94). Compared with the high physical activity and low WC-for-BMI, having medium or low levels of total physical activity, MVPA and VPA was associated with higher risk for incident CVD irrespective of abdominal adiposity. Having a higher WC-for-BMI was not associated with increased risk of CVD in those with high levels of MVPA (median=512 min/week) and VPA (median=32 min/week). Model 3 exhibited similar patterns, although less pronounced associations.

## Joint associations between general adiposity and physical activity with CVD

A clear dose–response association between BMI and risk of CVD was found in all strata of physical activity in joint associations between physical activity and general adiposity as measured by BMI (online supplemental figure 4). High levels of physical activity attenuated but did not offset the association from having overweight or obesity. Being normal weight was associated with higher risk in those with low levels of total physical activity (HR 1.21; 95% CI 1.02 to 1.43) and low VPA (HR 1.24; 95% CI 1.06 to 1.47). Obesity combined with low MVPA was associated with the highest risk (HR 2.03; 95% CI 1.75 to 2.36).

## Supporting and sensitivity analyses

Results from the analyses stratified by physical activity levels aligned with joint associations analyses, indicating that high levels of total physical activity, LPA, MVPA and VPA mitigated the risk associated with abdominal obesity and high WC-for-BMI (online supplemental tables 4 and 5). Whereas medium levels of VPA also offset the association in people with abdominal obesity and high WC-for-BMI, individuals with medium MVPA and LPA remained at 17%–27% higher risk. The patterns for the joint associations between WC and physical activity with incident CVD were similar in men and women. However, the effect sizes appeared greater in magnitude in women compared with men (online supplemental tables 6 and 7). Repeating the analysis of WHO cut-offs without adjustment for BMI accentuated associations and high levels of physical activity no longer offset the association between abdominal obesity and CVD (online

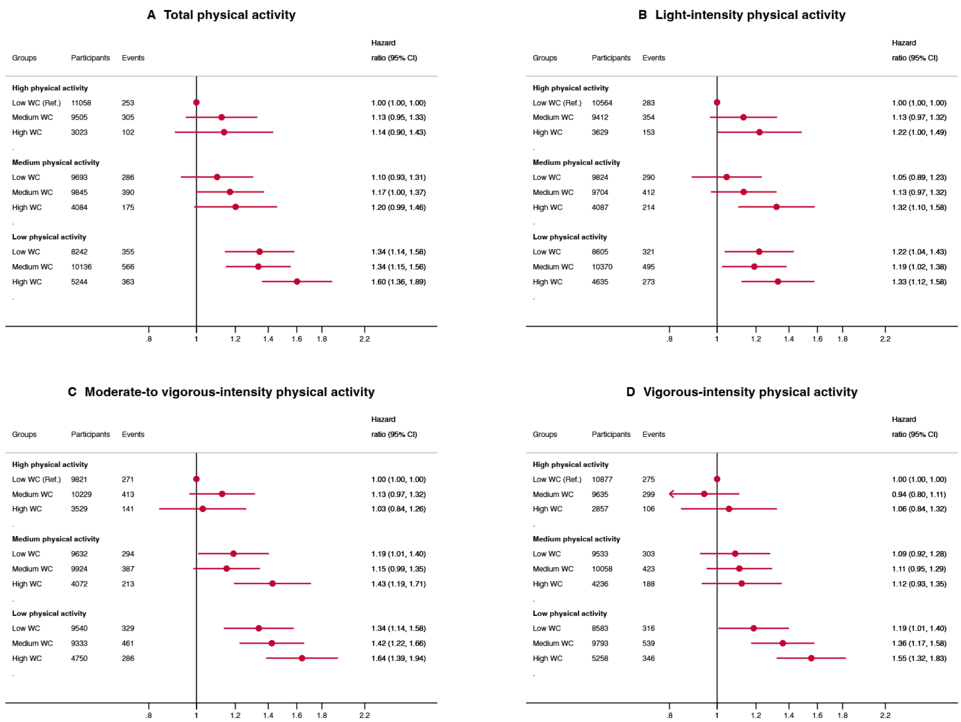



**Figure 2** Joint associations between categories of waist circumference (WC)-for-body mass index residuals, physical activity tertiles and incident cardiovascular disease. Ref: reference. Figure shows tertiles of weekly volumes of (A) total physical activity, (B) light-intensity, (C) moderate-to-vigorous intensity and (D) vigorous-intensity physical activity. Median (range) of physical activity levels for high, medium and low tertiles were, for total physical activity, 35.9 (31.0–97.2), 27.7 (24.7–31.0) and 21.4 (5.9–24.7) m*g*, respectively. For light-intensity min/week, 2794.3 (2390.4–5799.5), 2089.1 (1808.1–2390.3) and 1489.0 (28.0–1808.0). For moderate-to-vigorous intensity min/week, 511.9 (349.2–2999.7), 247.1 (164.1–349.1) and 87.5 (0.0–164.0). For vigorous-intensity min/week, 31.7 (13.1–756.7), 6.1 (2.8–13.0) and 1.0 (0.0–2.7). Results are from main model, adjusted for age (as timescale), sex, body mass index, ethnicity, education, living with partner, employment, Townsend Index, diet quality, alcohol intake, smoking and depression.

supplemental figure 5). The sensitivity analysis excluding the first 5 years of follow-up showed similar patterns but generally attenuated associations between higher WC and risk of CVD (online supplemental figure 6).

## DISCUSSION

Our results suggest that physical activity of any intensity can mitigate or even offset the association between abdominal obesity and incident CVD. Approximately 30–35 min per week of VPA appear to effectively offset the association of abdominal obesity with incident CVD.

Although high levels of LPA appear to attenuate the risk, the magnitude of associations were markedly stronger for MVPA and, particularly, for VPA. Indeed, as much as approximately 500 min per week of MVPA appear needed to fully offset the association with incident CVD.

Our results extend previous observations examining associations between VPA and risk for incident CVD[10 11] by modelling these associations in combination with proxies of abdominal adiposity. The observation that relatively small amounts of VPA offset the association was consistent both when analysing abdominal adiposity using WHO's WC cut-offs and when using WC-for-BMI residuals. We also found that being categorised in the lowest tertile of any physical activity intensity was associated with an increased risk of incident CVD, even when abdominal adiposity was low. Encouraging people with low levels of physical activity to engage in small amounts of VPA may be more appealing compared with large amounts of MVPA to reduce the risk of incident CVD.

We observed that high levels of physical activity were beneficial regardless of BMI strata. However, higher general adiposity, particularly obesity (BMI>30 kg/m$^2$), was associated with higher risk of incident CVD irrespective of physical activity. This finding corroborates previous observations from self-reported physical activity data and CVD mortality in women.[23] However, recent evidence suggests that high levels of self-reported physical activity may eliminate the risk of CVD mortality in people with grade I obesity (BMI 30–35 kg/m$^2$), but not in those with grade II (≥35 kg/m$^2$).[15] Insufficient statistical power prevented us from analysing associations by obesity grades. Further investigation is needed to determine the extent to which physical activity can mitigate CVD risk across different levels of obesity.

Measurements of WC do not distinguish between subcutaneous and visceral adipose tissue, both metabolically active.[24] During physical activity, subcutaneous adipose tissue in the upper body exhibits high lipolytic rates,[25] while the lower body contributes minimally,[26] and fatty acids used by active muscles mainly originate from subcutaneous abdominal fat.[27] The BMI includes lower-body subcutaneous fat tissue that may act as a metabolic buffer and protect other tissues from lipotoxicity caused by excess lipids and ectopic fat.[28] Moreover, individual variation in visceral adipose tissue exists for individuals with similar BMI, potentially explaining the variability in CVD risk profiles.[2] Thus, it is plausible that physical activity may more effectively mitigate the association between abdominal adiposity and incident CVD compared with total adiposity, particularly when the latter is assessed by BMI. This may also clarify the stronger associations observed between joint WC-physical activity categories and CVD without BMI adjustment (online supplemental figure 5) compared with the analysis with BMI adjustment (figure 1).

Our results may inform future physical activity recommendations. Current recommendations, primarily based on self-reported physical activity, suggest that 150–300 min of MVPA or 75–150 min of VPA or a combination of both is associated with substantial health benefits. This recommendation considers the same health benefits for half the amount of VPA compared with MVPA. Our results, as well as those from others,[11 29] challenge this concept. We found that approximately 15 times more MVPA was needed to mitigate the association between abdominal adiposity with incident CVD compared with VPA. This difference may be explained by the higher intensity physical activity leading to improvements in cardiorespiratory fitness, a strong marker of cardiovascular health that has been shown to modify the association between obesity and mortality, also known as the fat-but-fit paradox.[30–32] Previous studies have demonstrated that small bouts of VPA can improve cardiorespiratory fitness and have positive cardiovascular effects that may be greater than those from moderate-intensity activity.[33–36] Altogether, our results challenge the notion that substituting half the amount of MVPA with VPA maintains equal health benefits. Future guidelines may prioritise promoting the achievement of small amounts of VPA as a more feasible and time-effective strategy to counteract the CVD risk from abdominal obesity.

Our study's main strength lies in the inclusion of a large sample with WC and BMI measurements performed by clinical staff, reducing self-report bias.We categorised both central (WC) and total adiposity (BMI) based on WHO cut-offs, easily and routinely assessed by clinicians, enabling direct implementation of our findings in clinical practice. To investigate the independent associations of WC with CVD, we adjusted for BMI to isolate the specific contribution of abdominal adiposity to CVD risk.[6] Furthermore, we performed additional analyses using a variable based on WC-for-BMI residuals that confirmed the robustness of our findings. We measured physical activity by wrist-worn accelerometers, which is more accurate than self-report. However, physical activity levels derived from wrist-worn accelerometers are substantially higher than that from waist worn accelerometers.[37] Thus, absolute levels of time spent in moderate and vigorous-intensity and their associations with clinical outcomes are not directly comparable between studies employing different monitor placements.

## Limitations

Limitations of our study include the use of WC and the BMI as proxy measures of abdominal and total adiposity, respectively. Also, we used a single baseline assessment of adiposity and covariates, as well as a single accelerometer measurement that was performed about 5 years later. In subsamples of 16 230 and 15 854 participants with repeated WC and BMI assessments in 2014, we observed relatively stable adiposity measures, with 84% remaining in the same WC category and 78% in the same BMI category compared with their baseline measurements. However, we were unable to adjust for potential changes in exposures and covariates. The single measurement of physical activity also limits inference on individual variability of physical activity over time. To mitigate the risk of reverse causation, we excluded participants with prevalent diseases, mobility limitations and events occurring within the initial 2 years of follow-up (5 years in the sensitivity analysis). However, this may not completely eliminate this bias.[38] We also performed multivariate adjustment for numerous potential confounders, but residual bias from unmeasured or insufficiently measured confounders, such as smoking volume, intensity or duration, may still be present. Additionally, UK Biobank is not representative of its source population and there is evidence of healthy volunteer selection bias,[39] which may be accentuated in the subgroup with accelerometer measurements.[10]

## Implications for clinical practice and health policy

People living with obesity face difficulties in attaining and maintaining weight loss and in physical activity participation.[40] Our results imply that public health messaging should focus on achieving small amounts of VPA for reducing the risk of incident CVD, instead of only focusing on 'a number on a scale'. This may be especially attractive for those with limited time or motivation for more structured exercise.[36]

## Future directions

Future studies should use more precise measures of adiposity, such as DXA scans or MRI, to further explore how physical activity, preferably long-term patterns, can reduce the detrimental effect of excess adipose tissue on CVD risk. Studying the role of intramuscular fat and lean mass tissue's quality and volume in these associations could also provide valuable insights.[41] Additional research may want to include accelerometers attached to other body parts (eg, waist, thigh) to determine potential differences in the amount of physical activity needed to mitigate the risk for incident CVD associated with adiposity compared with the results from wrist-worn devices.

## CONCLUSION

Physical activity equivalent to approximately 30–35 min of vigorous intensity per week, measured by wrist-worn accelerometers, appears to offset the association between abdominal obesity and incident CVD. A considerably greater amount of physical activity of at least moderate intensity, approximately 500 min per week, is needed to achieve similar results.

**Author affiliations**
[1]Department of Sports Medicine, Norwegian School of Sports Sciences, Oslo, Norway
[2]Department of Special Didactics, University of Vigo Faculty of Education and Sports Sciences, Pontevedra, Spain
[3]Wellness and Movement Research Group (WellMove), Galicia Sur Health Research Institute (IIS Galicia Sur), SERGAS-UVIGO, Vigo, Spain
[4]Prevention Research Collaboration, The University of Sydney School of Public Health, Sydney, New South Wales, Australia
[5]The University of Sydney Charles Perkins Centre, Camperdown, New South Wales, Australia
[6]Department of Sports Science and Clinical Biomechanics, University of Southern Denmark Centre for Active and Healthy Ageing, Odense, Denmark
[7]University of Cadiz Faculty of Education Sciences, Puerto Real, Spain
[8]Biomedical Research and Innovation Institute of Cádiz (INiBICA) Research Unit, University of Cádiz Puerta del Mar University Hospital, Cádiz, Spain
[9]Department of Chronic Diseases, Norwegian Institute of Public Health, Oslo, Norway
[10]Department of Clinical Epidemiology, Aarhus University & University Hospital, Aarhus, Denmark

**Twitter** Miguel Adriano Sanchez-Lastra @adrianosanlas and Ding Ding @DrMelodyDing

**Acknowledgements** This research received no financial assistance. MAS-L was funded by the Spanish Ministry of Universities under application 33.50.460A.752 and by the European Union NextGenerationEU/PRTR through a Margarita Salas contract of the University of Vigo. DD was funded by a National Health and Medical Research Council Emerging Leader Grant (Application ID 2009254). BDPC was supported by the Government of Andalusia, Research Talent Recruitment Programme (EMERGIA 2020/00158).

**Contributors** Study concept and design: MAS-L, JT and UE. Acquisition of data: MAS-L, UE and JT. Statistical analysis of the data: MAS-L and JT. Interpretation of the data: all authors. Drafting the manuscript: MAS-L, UE and JT. Critical revision of the manuscript for important intellectual contet: all authors. Study supervision: UE, JT. MAS-L is the study guarantor.

**Funding** The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

**Competing interests** None declared.

**Patient and public involvement** Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

**Patient consent for publication** Not applicable.

**Ethics approval** This study involves human participants and was approved by North West - Haydock Research Ethics Committee (ID 21/NW/0157). Participants gave informed consent to participate in the study before taking part.

**Provenance and peer review** Not commissioned; externally peer reviewed.

**Data availability statement** The UK Biobank database used in this study can be accessed by researchers on application (https://www.ukbiobank.ac.uk/register-apply/).

**Supplemental material** This content has been supplied by the author(s). It has not been vetted by BMJ Publishing Group Limited (BMJ) and may not have been peer-reviewed. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by BMJ. BMJ disclaims all liability and responsibility arising from any reliance placed on the content. Where the content includes any translated material, BMJ does not warrant the accuracy and reliability of the translations (including but not limited to local regulations, clinical guidelines, terminology, drug names and drug dosages), and is not responsible for any error and/or omissions arising from translation and adaptation or otherwise.



**ORCID iDs**
Miguel Adriano Sanchez-Lastra http://orcid.org/0000-0001-7457-3475
Ding Ding http://orcid.org/0000-0001-9850-9224
Borja Del Pozo Cruz http://orcid.org/0000-0003-3944-2212
Jakob Tarp http://orcid.org/0000-0002-9186-7077

## REFERENCES


1 World Health Organization. Cardiovascular diseases (CVDs). 2021. Available: https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds) [Accessed 27 Sep 2022].
2 Powell-Wiley TM, Poirier P, Burke LE, *et al*. Obesity and cardiovascular disease: a scientific statement from the American heart association. *Circulation* 2021;143:E984–1010.
3 Bray GA, Heisel WE, Afshin A, *et al*. The science of obesity management: an endocrine society scientific statement. *Endocr Rev* 2018;39:79–132.
4 Rao G, Powell-Wiley TM, Ancheta I, *et al*. Identification of obesity and cardiovascular risk in ethnically and racially diverse populations: a scientific statement from the American heart association. *Circulation* 2015;132:457–72.
5 Longo DL, Heymsfield SB, Wadden TA. Mechanisms, pathophysiology, and management of obesity. *N Engl J Med* 2017;376:254–66.
6 Ross R, Neeland IJ, Yamashita S, *et al*. Waist circumference as a vital sign in clinical practice: a consensus statement from the IAS and ICCR working group on visceral obesity. *Nat Rev Endocrinol* 2020;16:177–89.
7 Thyfault JP, Bergouignan A. Exercise and metabolic health: beyond skeletal muscle. *Diabetologia* 2020;63:1464–74.
8 Prince SA, Adamo KB, Hamel ME, *et al*. A comparison of direct versus self-report measures for assessing physical activity in adults: a systematic review. *Int J Behav Nutr Phys Act* 2008;5:56.
9 Chastin SFM, De Craemer M, De Cocker K, *et al*. How does light-intensity physical activity associate with adult cardiometabolic health and mortality? Systematic review with meta-analysis of experimental and observational studies. *Br J Sports Med* 2019;53:370–6.
10 Dempsey PC, Rowlands AV, Strain T, *et al*. Physical activity volume, intensity, and incident cardiovascular disease. *Eur Heart J* 2022;43:4789–800.
11 Ahmadi MN, Clare PJ, Katzmarzyk PT, *et al*. Vigorous physical activity, incident heart disease, and cancer: how little is enough *Eur Heart J* 2022;43:4801–14.
12 Mansournia MA, Collins GS, Nielsen RO, *et al*. A checklist for statistical assessment of medical papers (the CHAMP statement): explanation and elaboration. *Br J Sports Med* 2021;55:1009–17.
13 The UK Biobank. UK Biobank: protocol for a large-scale prospective epidemiological resource; 2007. Available: https://www.ukbiobank.ac.uk/wp-content/uploads/2011/11/UK-Biobank-Protocol.pdf [Accessed 23 Sep 2019].
14 World Health Organization. Waist circumference and waist-hip ratio: report of a WHO expert consultation, Geneva, 8-11 December 2008; 2011.
15 Sanchez-Lastra MA, Ding D, Dalene KEE, *et al*. Physical activity and mortality across levels of adiposity: a prospective cohort study from the UK Biobank. *Mayo Clin Proc* 2021;96:105–19.
16 Doherty A, Jackson D, Hammerla N, *et al*. Large scale population assessment of physical activity using wrist worn accelerometers: the UK biobank study. *PLoS ONE* 2017;12:e0169649.
17 Walmsley R, Chan S, Smith-Byrne K, *et al*. Reallocation of time between device-measured movement Behaviours and risk of incident cardiovascular disease. *Br J Sports Med* 2022;56:1008–17.
18 Hildebrand M, Van Hees VT, Hansen BH, *et al*. Age group comparability of raw accelerometer output from wrist- and hip-worn monitors. *Med Sci Sports Exerc* 2014;46:1816–24.
19 Bosco E, Hsueh L, McConeghy KW, *et al*. Major adverse cardiovascular event definitions used in observational analysis of administrative databases: a systematic review. *BMC Med Res Methodol* 2021;21:1–18.
20 Textor J, van der Zander B, Gilthorpe MS, *et al*. Robust causal inference using directed acyclic graphs: the R package "Dagitty" *Int J Epidemiol* 2016;45:1887–94.
21 Townsend P, Phillimore P, Beattie A. *Health and deprivation: inequality and the North*. Croom Helm Ltd, 1988.
22 Eastwood SV, Mathur R, Atkinson M, *et al*. Algorithms for the capture and adjudication of prevalent and incident diabetes in UK biobank. *PLoS One* 2016;11:e0162388.
23 Hu FB, Willett WC, Li T, *et al*. Adiposity as compared with physical activity in predicting mortality among women. *N Engl J Med* 2004;351:2694–703.
24 Bjørndal B, Burri L, Staalesen V, *et al*. Different adipose depots: their role in the development of metabolic syndrome and mitochondrial response to hypolipidemic agents. *J Obes* 2011;2011:490650.
25 Arner P, Kriegholm E, Engfeldt P, *et al*. Adrenergic regulation of lipolysis in situ at rest and during exercise. *J Clin Invest* 1990;85:893–8.
26 Horowitz JF, Klein S. Oxidation of nonplasma fatty acids during exercise is increased in women with abdominal obesity. *J Appl Physiol (1985)* 2000;89:2276–82.
27 Horowitz JF. Fatty acid mobilization from adipose tissue during exercise. *Trends Endocrinol Metab* 2003;14:386–92.
28 Neeland IJ, Poirier P, Després JP. The cardiovascular and metabolic heterogeneity of obesity: clinical challenges and implications for management. *Circulation* 2018;137:1391–406.
29 Wang Y, Nie J, Ferrari G, *et al*. Association of physical activity intensity with mortality: a national cohort study of 403 681 US adults. *JAMA Intern Med* 2021;181:203–11.
30 Babu AS, Arena R, Myers J. Post-COVID era: time to re-introduce "cardiorespiratory fitness" as a vital sign. *EClinicalMedicine* 2022;51:101546.
31 Tarp J, Grøntved A, Sanchez-Lastra MA, *et al*. Fitness, fatness, and mortality in men and women from the UK biobank: prospective cohort study. *JAHA* 2021;10.
32 Ortega FB, Ruiz JR, Labayen I, *et al*. The fat but fit paradox: what we know and don't know about it. *Br J Sports Med* 2018;52:151–3.
33 Allison MK, Baglole JH, Martin BJ, *et al*. Brief intense stair climbing improves cardiorespiratory fitness. *Med Sci Sports Exerc* 2017;49:298–307.
34 Jenkins EM, Nairn LN, Skelly LE, *et al*. Do stair climbing exercise "snacks" improve cardiorespiratory fitness *Appl Physiol Nutr Metab* 2019;44:681–4.
35 Franklin BA, Eijsvogels TMH, Pandey A, *et al*. Physical activity, cardiorespiratory fitness, and cardiovascular health: a clinical practice statement of the American society for preventive cardiology part II: physical activity, cardiorespiratory fitness, minimum and goal intensities for exercise training, prescriptive methods, and special patient populations. *Am J Prev Cardiol* 2022;12:100425.
36 Stamatakis E, Ahmadi MN, Gill JMR, *et al*. Association of Wearable device-measured vigorous intermittent lifestyle physical activity with mortality. *Nat Med* 2022;28:2521–9.
37 Loprinzi PD, Smith B. Comparison between wrist-worn and waist-worn accelerometry. *J Phys Act Health* 2017;14:539–45.
38 Tarp J, Hansen BH, Fagerland MW, *et al*. Accelerometer-measured physical activity and sedentary time in a cohort of US adults followed for up to 13 years: the influence of removing early follow-up on associations with mortality. *Int J Behav Nutr Phys Act* 2020;17:39.
39 Fry A, Littlejohns TJ, Sudlow C, *et al*. The representativeness of the UK biobank cohort on a range of sociodemographic, physical, lifestyle and health-related characteristics. *J Epidemiol Community Health* 2016;70:A26.
40 Wharton S, Lau DCW, Vallis M, *et al*. Obesity in adults: a clinical practice guideline. *CMAJ* 2020;192:E875–91.
41 Zamboni M, Gattazzo S, Rossi AP. Myosteatosis: a relevant, yet poorly explored element of sarcopenia. *Eur Geriatr Med* 2019;10:5–6.

# SUPPLEMENTARY FILES
## Joint associations of device-measured physical activity and abdominal obesity with incident cardiovascular disease: a prospective cohort study

**Supplementary Table 1.** Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist of items that should be included in reports of cohort studies.

| | Item No | Recommendation | Location |
|---|---|---|---|
| **Title and abstract** | 1 | (*a*) Indicate the study's design with a commonly used term in the title or the abstract | Title page (page 1) |
| | | (*b*) Provide in the abstract an informative and balanced summary of what was done and what was found | Abstract (page 3) |
| **Introduction** | | | |
| Background/rationale | 2 | Explain the scientific background and rationale for the investigation being reported | Introduction, paragraphs 1-4 (page 6) |
| Objectives | 3 | State specific objectives, including any prespecified hypotheses | Introduction, last paragraph (page 6-7) |
| **Methods** | | | |
| Study design | 4 | Present key elements of study design early in the paper | Methods, *Data source and study population* subsection (page 7) |
| Setting | 5 | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection | Methods, *Data source and study population* subsection (page 7) |
| Participants | 6 | (*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up | Methods, *Data source and study population* (page 7) *Analytical sample* (page 10), and *Statistical analyses* (pages 10-11) subsections |
| | | (*b*) For matched studies, give matching criteria and number of exposed and unexposed | Not applicable |
| Variables | 7 | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable | Methods, *Exposures* (pages 5-6), *Incident CVD* (pages 6-7), and *Covariates* (page 7) subsections |
| Data sources/ measurement | 8* | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group | Methods, *Exposures* (pages 7-8), *Incident CVD* (pages 8-9), and *Covariates* (pages 9-10) subsections; Supplementary Table 1 |
| Bias | 9 | Describe any efforts to address potential sources of bias | Methods, *Statistical analyses* subsection (pages 10-11) |
| Study size | 10 | Explain how the study size was arrived at | Methods, *Analytical sample* subsection (page 10) |
| Quantitative variables | 11 | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why | Methods, *Statistical analyses* subsection (pages 10-11); Supplementary Table 1 |
| Statistical methods | 12 | (*a*) Describe all statistical methods, including those used to control for confounding | Methods, *Statistical analyses* subsection (pages 10-11) |
| | | (*b*) Describe any methods used to examine subgroups and interactions | Methods, *Statistical analyses* subsection (pages 10-11) |
| | | (*c*) Explain how missing data were addressed | Methods, *Analytical sample* subsection (page 10) |
| | | (*d*) If applicable, explain how loss to follow-up was addressed | Methods, *Analytical sample* (page 10) and *Statistical analyses* (pages 10-11) subsections |
| | | (*e*) Describe any sensitivity analyses | Methods, *Statistical analyses* subsection (pages 10-11) |
| **Results** | | | |
| Participants | 13* | (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed | Results, first paragraph (page 12); Supplementary Figure 2 |

| | | | |
|---|---|---|---|
| | | (b) Give reasons for non-participation at each stage | Supplementary Figure 2 |
| | | (c) Consider use of a flow diagram | Supplementary Figure 2 |
| Descriptive data | 14* | (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders | Table 1; Supplementary Figure 1; Supplementary Table 3 |
| | | (b) Indicate number of participants with missing data for each variable of interest | Supplementary Figure 2 |
| | | (c) Summarise follow-up time (eg, average and total amount) | Results, first paragraph (page 12) |
| Outcome data | 15* | Report numbers of outcome events or summary measures over time | Results, first paragraph (page 12) |
| Main results | 16 | (*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included | Results, pages 12-13 |
| | | (*b*) Report category boundaries when continuous variables were categorized | Table 1; Table 2; Supplementary Table 3 |
| | | (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period | Not applicable |
| Other analyses | 17 | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses | Results (pages 14-15) and Supplementary files |
| **Discussion** | | | |
| Key results | 18 | Summarise key results with reference to study objectives | Discussion , first paragraph (page 15) |
| Limitations | 19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias | Discussion, L*imitations* subsection (page 18) |
| Interpretation | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence | Discussion, pages 15-19 |
| Generalisability | 21 | Discuss the generalisability (external validity) of the study results | Discussion, *Implications for clinical practice and health policy* subsection (page 18) |
| **Other information** | | | |
| Funding | 22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based. | Page 20 |

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

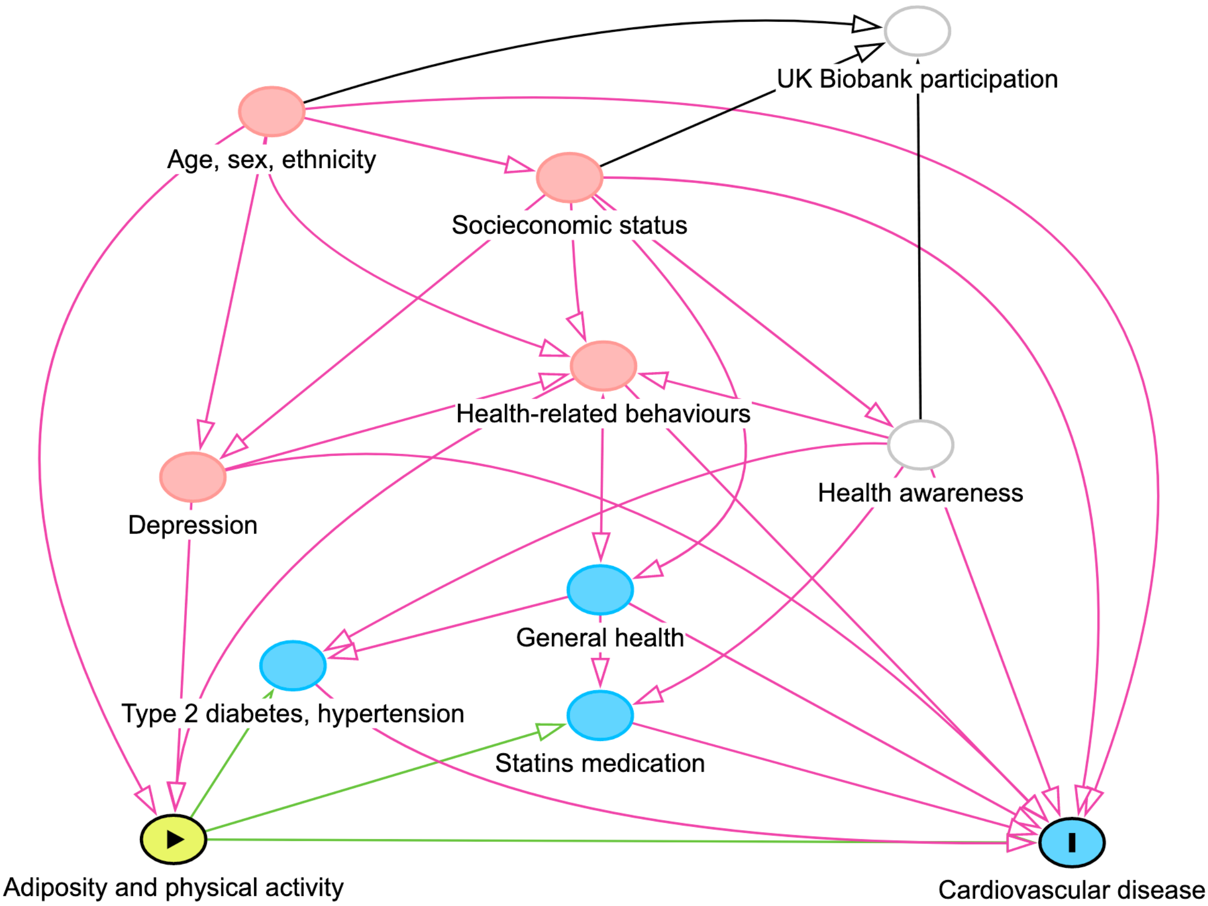
**Supplementary Table 2.** Description of variables used and data processing from the UK Biobank data showcase.

| Variable | Data processing | Used UK Biobank field/s |
|---|---|---|
| Light intensity physical activity (minutes per week) | Overall average proportion of time spent doing light intensity activity across the monitoring period, based on machine-learning methods, multiplied by 10,080 minutes per week, and categorized in tertiles. | 40048 |
| Vigorous intensity physical activity (minutes per week) | Overall average proportion of time spent in accelerations above 400 *mg* across the monitoring period, multiplied by 10,080 minutes per week, and categorized in tertiles. | Variable *cutPointVPA-overall-avg* in Return 2040 |
| Moderate-to-vigorous intensity physical activity (minutes per week) | Overall average proportion of time spent doing moderate-to-vigorous intensity activity across the monitoring period, based on machine-learning methods, multiplied by 10,080 minutes per week, and categorized in tertiles. | 40049 |
| Total physical activity per week | Direct categorization of overall acceleration average (*mg*) in tertiles | 90012 |
| Body Mass Index | From measured height and weight and categorized as normal weight (18.5-24.9 kg/m$^2$), overweight (25-29.9 kg/m$^2$) and obese (≥30 kg/m$^2$). | 21001 |
| Waist Circumference | For clinical categories: Categorization as low (if below 88 cm in women and 102 cm in men) or high (equal-to or above the cut-offs).<br><br>For categories based on WC-for-BMI residuals: Using the residuals from regressing the waist circumference (cm) on the BMI (kg/m$^2$) and categorization as low, medium, and high, maintaining the sex-specific distribution in the BMI categories. | 48, 21001 |
| Incident cardiovascular disease (fatal and non-fatal) | Cardiovascular death (ICD-10 codes I00-I99) or the first hospital diagnosis of ischemic heart disease (ICD-10 codes I20-25), heart failure (I50) or stroke (I60-I64). | 41270, 41280 |
| Follow-up | From date when the participants stopped wearing the accelerometer to incident CVD, death, or lost to follow-up. | 41280, 90011, 191, 30 |
| Age | Difference between date of birth and date when they stopped wearing the accelerometer | 34 |
| Sex | Men/women | 31 |
| Townsend deprivation index | Marker of area-based socioeconomic status, derived from postcode of residence and census data on housing, employment, social class, and car availability | 189 |
| Ethnicity | White, Asian, Black, Others | 21000 |
| Education | No qualifications, not college or university degree, and college or university degree | 6138 |
| Living/not living with partner | Yes/no | 709, 6414 |

| | | |
|---|---|---|
| Dietary Quality | Meeting or not each recommendation: 1) ≤3 weekly servings of red meat and ≤1 servings/week of processed meat; 2) ≥2 servings per week of fish, at least one as oily fish; 3) ≥400 grams per day of fruits and vegetables. Meeting each recommendation is 1 point. | Oily fish: 1329<br>Non-oily fish:1339<br>Fruit/vegetable:1289,1299, 1309, 1319<br>Processed meat: 1349<br>Red meat:1369, 1379, 1389 |
| Alcohol intake | Never, previous, current and <3 times/week, and current and ≥3 times/week | 20117, 1558 |
| Smoking | Never, previous, current smoker | 20160 |
| Employment | Employed, unemployed, retired | 6142 |
| History of depression | Yes/no. | 20002 |
| Prevalent diabetes | Yes/no | Algorithm from Eastwood et al. 2016: https://doi.org/10.1371/journal.pone.0162388 |
| Hypertension | Yes/no. Combination of:<br>Self-reported high blood Pressure, self-reported blood pressure medication<br>Measured, manual or automated systolic and diastolic blood pressure<br>Self-reported hypertension, essential hypertension. | 6150, 6153 (women), 6177 (men), 4080, 4079, 93, 94, 20002 |
| Statins medication | Yes/no | 20003 |
| Anorexia, bulimia or other eating disorder | Anorexia/bulimia/other eating disorder | 20002 |
| Attendance/disability/mobility allowance | Attendance, disability or mobility allowance | 6146 |
| Prevalent cancer (by the end of the accelerometer assessment) | Categorization: yes/no<br>Sources:<br>(Questionnaire) self-reported<br>(Interview) self-reported cancer excluding non-melanoma skin cancer<br>(Cancer Registry) Any cancer-type<br>(C-D48) excluding non-melanoma skin cancers (ICD-10; C44, ICD-9; 173) | 2453, 20001, 40006 |
| Prevalent CVD (by the end of the accelerometer assessment) | Categorization: yes/no<br>Sources:<br>(Algorithmically defined outcomes)<br>Myocardial infarction (ICD-10 codes I21, I22, I23, I24.1, I25.2, and ICD-9 codes 410, 411, 412.X, 429.79)<br>Stroke (ICD-10 codes I60, I61, I63, I64, and ICD-9 codes 430.X, 431.X, 434.X, 434.0, 434.1, 434.9, 436.X)<br>(Hospital inpatient data)<br>Angina (ICD-10 codes I20.0, I20.1, I20.8, I20.9, and ICD-9 code 4139)<br>Heart failure (ICD-10 codes I11.0, I11.9, I13.0, I13.2, I13.9, I50.0, I50.1, I50.9, and ICD-9 codes 4280, 4281, 4289) | 42000, 42006 |

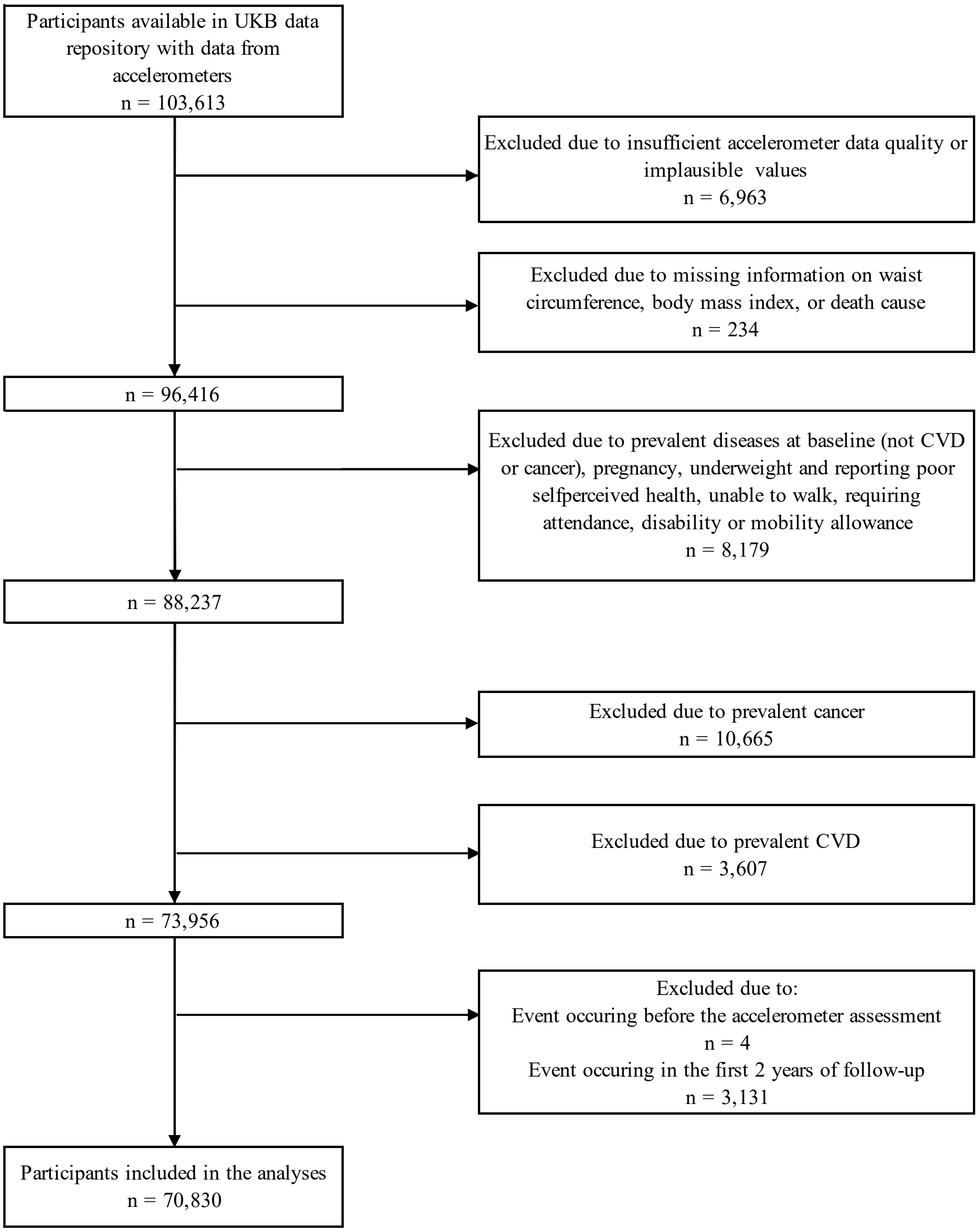
| | | |
|---|---|---|
| Chronic immunological or sistemic diseases | yes/no<br>Sources:<br>(Interview) Self-reported rheumatoid arthritis, vasculitis, giant cell/temporal arteritis, polymyalgia rheumatica, Wegners granulmatosis, microscopic polyarteritis, polyartertis nodosa, systemic lupus erythematosis/sle, sjogren's syndrome/sicca syndrome, dermatopolymyositis, dermatomyositis, polymyositis, scleroderma/systemic sclerosis, chronic fatigue syndrome, antiphospholipid syndrome | 20002_0_0 – 20002_0_28 |
| Chronic respiratory diseases (not including Chronic obstructive pulmonary disease) | yes/no<br>Sources:<br>(Interview) Self-reported bronchiectasis, interstitial lung disease, asbestosis, pulmonary fibrosis, fibrosing alveolitis/unspecified alveolitis, respiratory failure | 20002_0_0 – 20002_0_28 |
| Chronic widespread pain | yes/no<br>Sources:<br>(Questionnaire) "Have you had pains all over the body for more than 3 months?" | 2956_0_0 |
| Chronic/degenerative neurological problem | yes/no<br>Sources:<br>(Interview) self-reported chronic/degenerative neurological problem, Parkinson's disease, dementia/Alzheimer's/cognitive impairment, motor neuron disease, myasthenia gravis, multiple sclerosis, other demyelinating disease (not multiple sclerosis) | 20002_0_0 – 20002_0_28 |
| Chronic obstructive pulmonary disease | yes/no<br>Sources:<br>Algorithmically defined outcomes and COPD from self-report or hospital admission | 42016 |
| Liver failure/cirrhosis | yes/no<br>Sources:<br>(Interview) self-reported liver failure/cirrhosis, primary biliary cirrhosis, alcoholic liver disease / alcoholic cirrhosis | 20002 |
| Pregnancy | yes/no<br>Sources: (interview) | 3140 |
| Psychological or psychriatic problems | yes/no<br>Sources:<br>(Interview) self-reported schizophrenia, mania/bipolar disorder/manic depression, deliberate self-harm/suicide attempt, post-traumatic stress disorder | 20002 |
| Substance abuse/dependency | yes/no<br>Sources:<br>(Interview) self-reported alcohol dependency, opioid dependency, other substance abuse/dependency | 20002 |

**Supplementary Figure 1.** Directed acyclic diagram of the association under study.




Health-related behaviors include sedentary time, diet pattern, smoking, alcohol intake. Socioeconomic status include education, marital status, employment status and Townsend deprivation index. Direct arrows from ethnicity and sex to physical activity/adiposity represent potential influences of unmeasured societal factors (e.g., feeling of insecurity to be physically active at night or in some places, religious beliefs conditioning education and not covered by our education variable, etc). Direct arrow from socioeconomic status to cardiovascular disease represent other unmeasured/additional health-related exposures not only mediated by awareness, like unhealthy factors at work or in the area of living, having access to places to be physically active, etc).

**Supplementary Figure 2.** Flowchart of the inclusion and exclusion process. Exclusions due to prevalent diseases at baseline included cancer (excluding non-melanoma skin cancer), cardiovascular diseases, chronic neurological degenerative problems, widespread pain, respiratory diseases (including chronic obstructive pulmonary disease), liver failure or cirrhosis, psychological or psychiatric problems, substance abuse or dependency, or eating disorders.

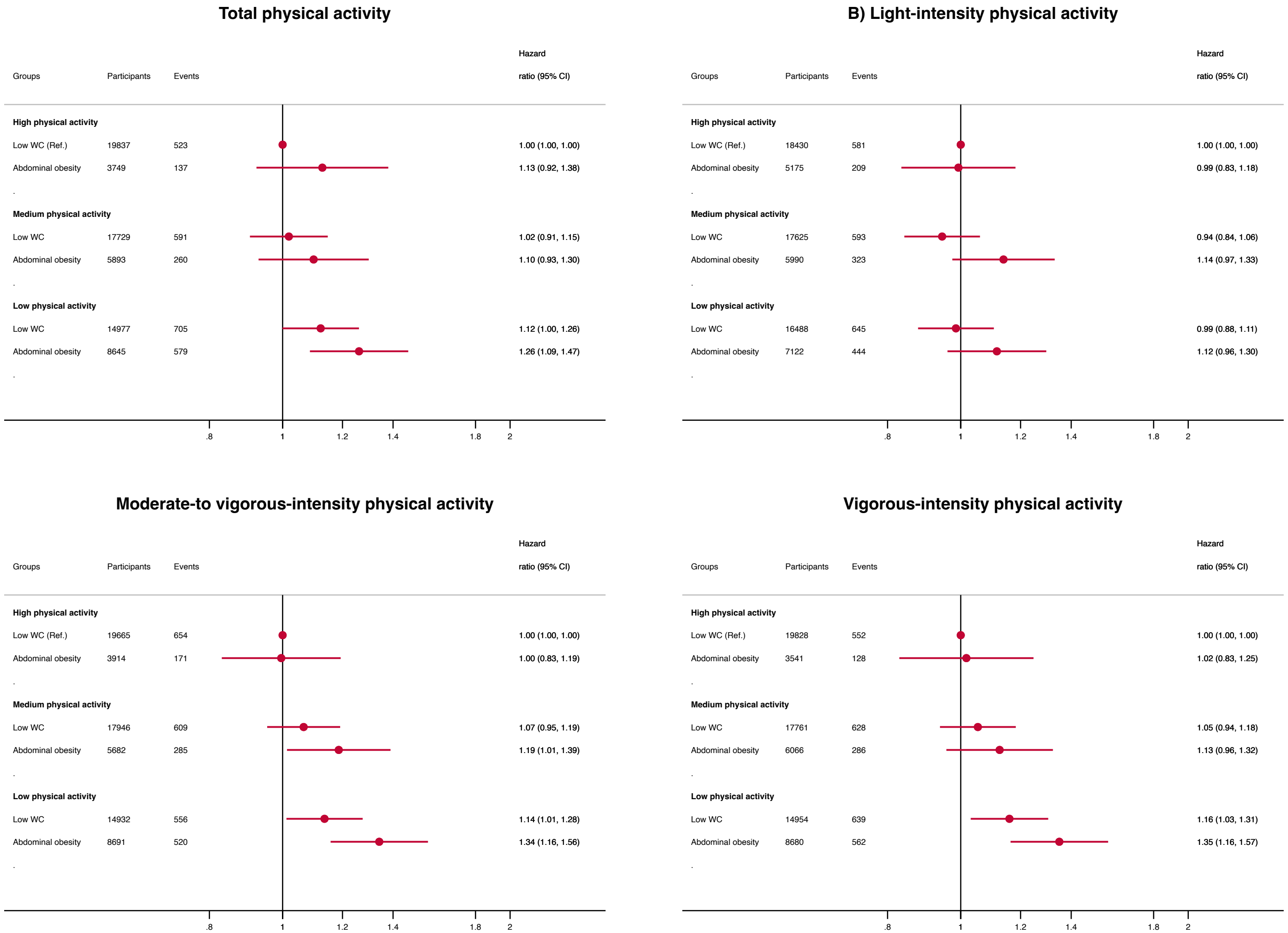


**Supplementary Table 3.** Descriptive physical activity and sedentary time data in the total sample, by physical activity tertiles, and waist circumference categories based on the World Health Organization's cut-off points.

| | **Total sample** | **Physical activity tertiles** | | | **Waist circumference categories** | |
|---|---|---|---|---|---|---|
| | | **Low** | **Medium** | **High** | **Low** | **Abdominal obesity** |
| Total volume of physical activity (average acceleration, mg) | 27.7 (5.9-97.2) | 21.4 (5.9-24.7) | 27.7 (24.7-31.0) | 35.9 (31.0-97.2) | 28.6 (7.7-97.21) | 25.15 (5.9-89.5) |
| Light-intensity physical activity (minutes/week) | 2089.0 (28.0-5799.5) | 1489.0 (28.0-1808.0) | 2089.1 (1808.1-2390.3) | 2794.3 (2390.4-5799.5) | 2122.2 (28.0-5799.5) | 1995.2 (47.0-5702.6) |
| Moderate-to-vigorous-intensity physical activity (minutes/week) | 247.0 (0.0-2999.7) | 87.5 (0.0-164.0) | 247.1 (164.1-349.1) | 511.9 (349.2-2999.7) | 273.1 (0.0-2999.7) | 174.5 (0.0-2388.3) |
| Vigorous-intensity physical activity (minutes/week) | 6.0 (0.0-756.7) | 1.0 (0.0-2.7) | 6.1 (2.8-13.0) | 31.7 (13.1-756.7) | 8.0 (0.0-756.7) | 3.0 (0.0-480.0) |

All values are median (range). Low waist circumference represents <88cm in women and <102 cm in men.

**Supplementary Figure 3.** Results from model 3 for the joint associations between waist circumenference (WC) categories based on World Health Organization's cut-off points, tertiles of physical activity, and incident cardiovascular disease. Model was adjusted for age (as timescale), sex, body mass index, ethnicity, education, living/not living with partner, employment, Townsend, diet quality, alcohol intake, smoking, depression, prevalent type 2 diabetes, hypertension, and use of statins medication. Low WC was defined as <88 cm in women and <102 cm of WC in men, and high otherwise.



**Supplementary Table 4.** Stratified associations between waist circumference (WC) categories from World Health Organization's cut-offs and incident cardiovascular disease by tertiles of physical activity.

| Groups | n total | n events | Hazard ratio (95% CI) |
|---|---|---|---|
| **Total physical activity** | | | |
| High | | | |
| Low WC | 19,837 | 523 | 1.00 (Reference) |
| Abdominal obesity | 3,749 | 137 | 1.13 (0.88, 1.45) |
| Medium | | | |
| Low WC | 17,729 | 591 | 1.00 (Reference) |
| Abdominal obesity | 5,893 | 260 | 1.04 (0.86, 1.27) |
| Low | | | |
| Low WC | 14,977 | 705 | 1.00 (Reference) |
| Abdominal obesity | 8,645 | 579 | 1.19 (1.03, 1.39) |
| **Light intensity physical activity** | | | |
| High | | | |
| Low WC | 18,430 | 581 | 1.00 (Reference) |
| Abdominal obesity | 5,175 | 209 | 1.12 (0.91, 1.40) |
| Medium | | | |
| Low WC | 17,625 | 593 | 1.00 (Reference) |
| Abdominal obesity | 5,990 | 323 | 1.20 (0.99, 1.45) |
| Low | | | |
| Low WC | 16,488 | 645 | 1.00 (Reference) |
| Abdominal obesity | 7,122 | 444 | 1.12 (0.95, 1.32) |
| **Moderate-to-vigorous intensity physical activity** | | | |
| High | | | |
| Low WC | 19,665 | 654 | 1.00 (Reference) |
| Abdominal obesity | 3,914 | 171 | 0.99 (0.79, 1.24) |
| Medium | | | |
| Low WC | 17,946 | 609 | 1.00 (Reference) |
| Abdominal obesity | 5,682 | 285 | 1.19 (0.98, 1.44) |
| Low | | | |
| Low WC | 14,932 | 556 | 1.00 (Reference) |
| Abdominal obesity | 8,691 | 520 | 1.19 (1.01, 1.40) |
| **Vigorous intensity physical activity** | | | |
| High | | | |
| Low WC | 19,828 | 552 | 1.00 (Reference) |
| Abdominal obesity | 3,541 | 128 | 1.01 (0.79, 1.31) |
| Medium | | | |
| Low WC | 17,761 | 628 | 1.00 (Reference) |
| Abdominal obesity | 6,066 | 286 | 1.01 (0.83, 1.22) |
| Low | | | |
| Low WC | 14,954 | 639 | 1.00 (Reference) |
| Abdominal obesity | 8,680 | 562 | 1.25 (1.07, 1.46) |

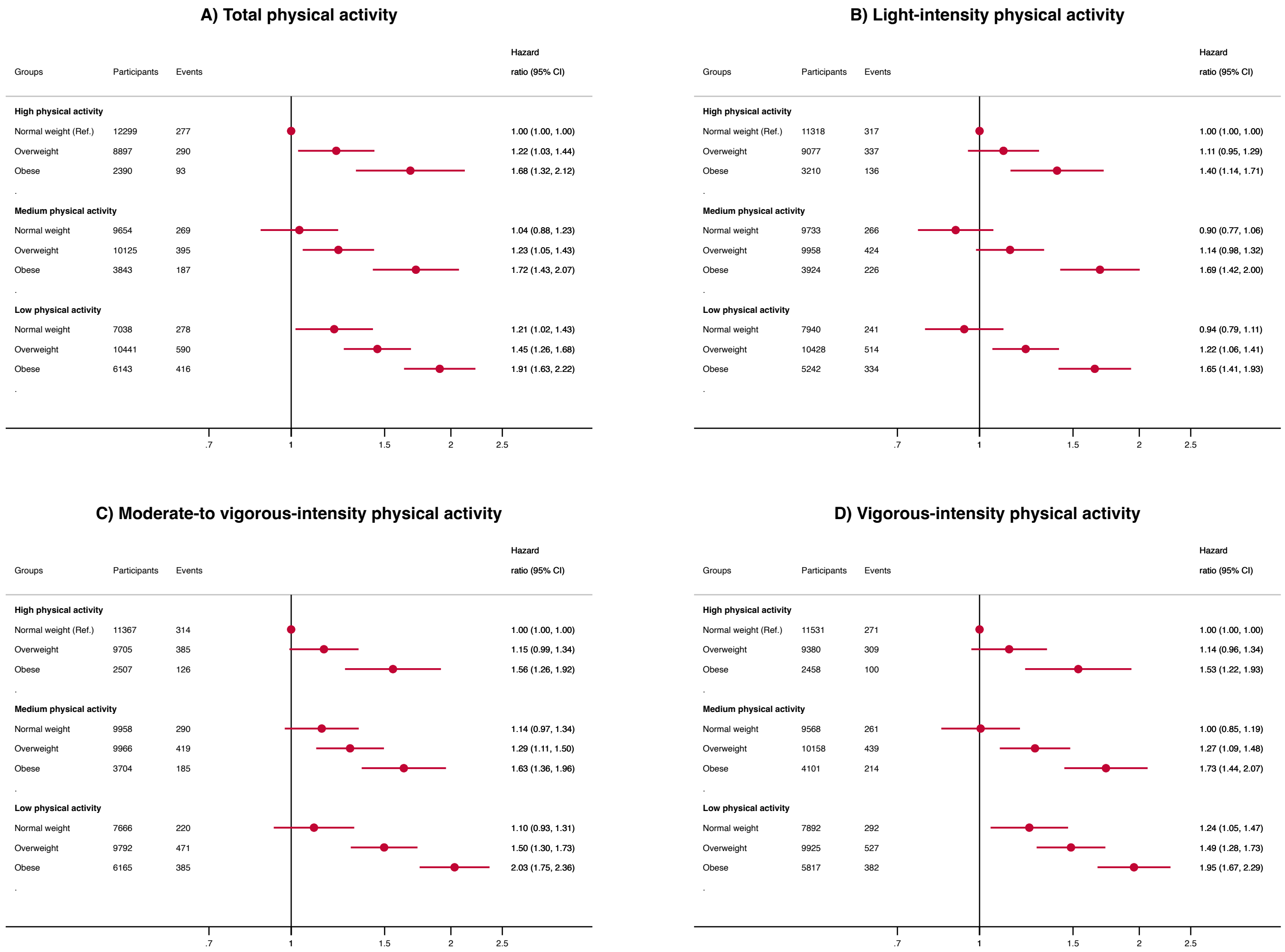
Results are from main model, adjusted for age (as timescale), sex, body mass index, ethnicity, education, living/not living with partner, employment, Townsend, diet quality, alcohol intake, smoking and depression.

**Supplementary Table 5.** Stratified associations between waist circumference (WC) categories of WC-for-BMI residuals and incident cardiovascular disease by tertiles of physical activity.

| Groups | n total | n events | Hazard ratio (95% CI) |
|---|---|---|---|
| **Total physical activity** | | | |
| High | | | |
| Low WC | 11,058 | 253 | 1.00 (Reference) |
| Medium WC | 9,505 | 305 | 1.11 (0.93, 1.31) |
| High WC | 3,023 | 102 | 1.13 (0.90, 1.43) |
| Medium | | | |
| Low WC | 9,693 | 286 | 1.00 (Reference) |
| Medium WC | 9,845 | 390 | 1.06 (0.91, 1.24) |
| High WC | 4,084 | 175 | 1.10 (0.91, 1.33) |
| Low | | | |
| Low WC | 8,242 | 355 | 1.00 (Reference) |
| Medium WC | 10,136 | 566 | 1.01 (0.88, 1.15) |
| High WC | 5,244 | 363 | 1.20 (1.03, 1.39) |
| **Light intensity physical activity** | | | |
| High | | | |
| Low WC | 10,564 | 283 | 1.00 (Reference) |
| Medium WC | 9,412 | 354 | 1.13 (0.96, 1.32) |
| High WC | 3,629 | 153 | 1.22 (1.00, 1.49) |
| Medium | | | |
| Low WC | 9,824 | 290 | 1.00 (Reference) |
| Medium WC | 9,704 | 412 | 1.08 (0.93, 1.26) |
| High WC | 4,087 | 214 | 1.27 (1.06, 1.52) |
| Low | | | |
| Low WC | 8,605 | 321 | 1.00 (Reference) |
| Medium WC | 10,370 | 495 | 0.98 (0.85, 1.13) |
| High WC | 4,635 | 273 | 1.09 (0.93, 1.28) |
| **Moderate-to-vigorous intensity physical activity** | | | |
| High | | | |
| Low WC | 9,821 | 271 | 1.00 (Reference) |
| Medium WC | 10,229 | 413 | 1.12 (0.96, 1.31) |
| High WC | 3,529 | 141 | 1.04 (0.84, 1.27) |
| Medium | | | |
| Low WC | 9,632 | 294 | 1.00 (Reference) |
| Medium WC | 9,924 | 387 | 0.95 (0.81, 1.11) |
| High WC | 4,072 | 213 | 1.17 (0.98, 1.40) |
| Low | | | |
| Low WC | 9,540 | 329 | 1.00 (Reference) |
| Medium WC | 9,333 | 461 | 1.08 (0.94, 1.25) |
| High WC | 4,750 | 286 | 1.24 (1.05, 1.46) |
| **Vigorous intensity physical activity** | | | |
| High | | | |
| Low WC | 10,877 | 275 | 1.00 (Reference) |
| Medium WC | 9,635 | 299 | 0.94 (0.79, 1.11) |
| High WC | 2,857 | 106 | 1.06 (0.84, 1.33) |
| Medium | | | |
| Low WC | 9,533 | 303 | 1.00 (Reference) |
| Medium WC | 10,058 | 423 | 1.00 (0.86, 1.17) |
| High WC | 4,236 | 188 | 1.03 (0.85, 1.23) |
| Low | | | |
| Low WC | 8,583 | 316 | 1.00 (Reference) |
| Medium WC | 9,793 | 539 | 1.16 (1.00, 1.33) |
| High WC | 5,258 | 346 | 1.32 (1.13, 1.54) |

Results are from main model, adjusted for age (as timescale), sex, ethnicity, education, living/not living with partner, employment, Townsend, diet quality, alcohol intake, smoking and depression.

**Supplementary Figure 4.** Joint associations between body mass index categories, tertiles of physical activity, and incident cardiovascular disease. Models were adjusted for age (as timescale), sex, ethnicity, education, living/not living with partner, employment, Townsend, diet quality, alcohol intake, smoking, and depression.



**Supplementary Table 6.** Sex-stratified joint associations between waist circumference (WC) categories from World Health Organization's cut-offs, physical activity tertiles, and incident cardiovascular disease.

| | Women | | | Men | | |
|---|---|---|---|---|---|---|
| **Groups** | **n total** | **n events** | **Hazard ratio (95% CI)** | **n total** | **n events** | **Hazard ratio (95% CI)** |
| **Total physical activity** | | | | | | |
| High | | | | | | |
| Low WC (reference) | 11,439 | 185 | 1.00 | 8,398 | 338 | 1.00 |
| Abdominal obesity | 2,420 | 58 | 1.14 (0.83, 1.56) | 1,329 | 79 | 1.20 (0.93, 1.56) |
| Medium | | | | | | |
| Low WC | 10,009 | 214 | 1.05 (0.86, 1.28) | 7,720 | 377 | 1.02 (0.88, 1.18) |
| Abdominal obesity | 3,750 | 117 | 1.18 (0.91, 1.53) | 2,143 | 143 | 1.11 (0.89, 1.38) |
| Low | | | | | | |
| Low WC | 7,421 | 215 | 1.18 (0.97, 1.45) | 7,556 | 490 | 1.15 (0.99, 1.32) |
| Abdominal obesity | 4,924 | 253 | 1.54 (1.21, 1.96) | 3,721 | 326 | 1.22 (1.01, 1.47) |
| **Light intensity physical activity** | | | | | | |
| High | | | | | | |
| Low WC (reference) | 12,646 | 290 | 1.00 | 5,784 | 291 | 1.00 |
| Abdominal obesity | 3,820 | 119 | 0.99 (0.78, 1.26) | 1,355 | 90 | 1.05 (0.81, 1.35) |
| Medium | | | | | | |
| Low WC | 10,022 | 211 | 0.94 (0.79, 1.12) | 7,603 | 382 | 0.95 (0.82, 1.11) |
| Abdominal obesity | 3,904 | 150 | 1.16 (0.92, 1.46) | 2,086 | 173 | 1.19 (0.96, 1.47) |
| Low | | | | | | |
| Low WC | 6,201 | 113 | 0.88 (0.70, 1.09) | 10,287 | 532 | 1.03 (0.89, 1.19) |
| Abdominal obesity | 3,370 | 159 | 1.42 (1.11, 1.81) | 3,752 | 285 | 1.07 (0.88, 1.29) |
| **Moderate-to-vigorous intensity physical activity** | | | | | | |
| High | | | | | | |
| Low WC (reference) | 8,477 | 145 | 1.00 | 11,188 | 509 | 1.00 |
| Abdominal obesity | 1,748 | 44 | 1.04 (0.73, 1.49) | 2,166 | 127 | 1.02 (0.82, 1.26) |
| Medium | | | | | | |
| Low WC | 10,429 | 215 | 1.05 (0.85, 1.29) | 7,517 | 394 | 1.10 (0.97, 1.26) |
| Abdominal obesity | 3,327 | 107 | 1.21 (0.92, 1.60) | 2,355 | 178 | 1.24 (1.02, 1.50) |
| Low | | | | | | |
| Low WC | 9,963 | 254 | 1.14 (0.93, 1.41) | 4,969 | 302 | 1.18 (1.02, 1.37) |
| Abdominal obesity | 6,019 | 277 | 1.49 (1.16, 1.91) | 2,672 | 243 | 1.33 (1.10, 1.61) |
| **Vigorous intensity physical activity** | | | | | | |
| High | | | | | | |
| Low WC (reference) | 9,378 | 141 | 1.00 | 10,450 | 411 | 1.00 |
| Abdominal obesity | 1,826 | 42 | 1.11 (0.77, 1.60) | 1,715 | 86 | 1.02 (0.79, 1.30) |
| Medium | | | | | | |
| Low WC | 9,685 | 201 | 1.04 (0.84, 1.30) | 8,076 | 427 | 1.09 (0.95, 1.24) |

| | | | | | | |
|---|---|---|---|---|---|---|
| Abdominal obesity | 3,431 | 91 | 1.02 (0.76, 1.36) | 2,635 | 195 | 1.26 (1.03, 1.53) |
| Low | | | | | | |
| Low WC | 9,806 | 272 | 1.10 (0.89, 1.35) | 5,148 | 367 | 1.27 (1.10, 1.47) |
| Abdominal obesity | 5,837 | 295 | 1.49 (1.17, 1.91) | 2,843 | 267 | 1.33 (1.10, 1.61) |

Results are from main model, adjusted for age (as timescale), body mass index, ethnicity, education, living/not living with partner, employment, Townsend, diet quality, alcohol intake, smoking and depression.

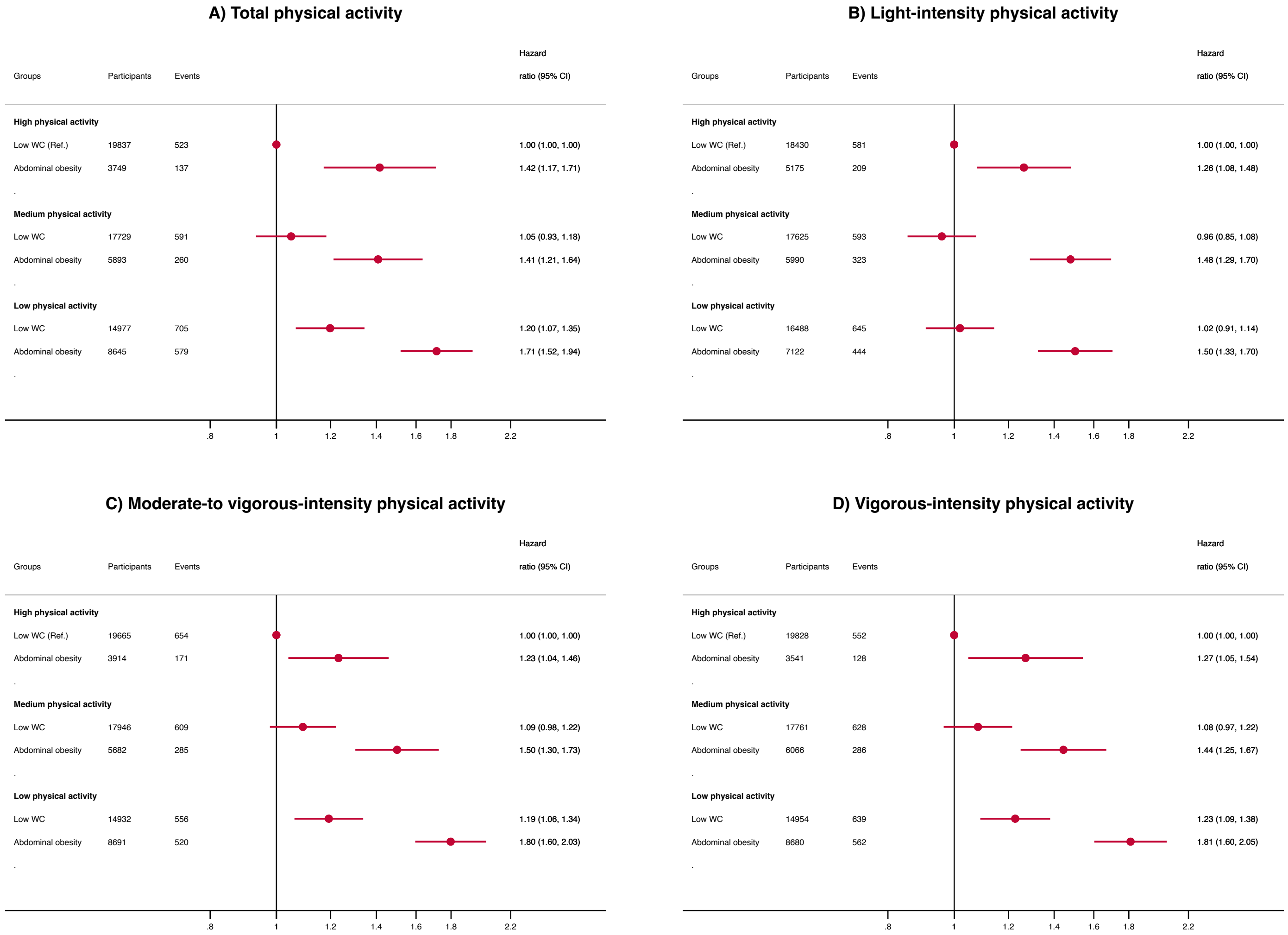
**Supplementary Table 7.** Sex-stratified joint associations between waist circumference (WC) categories of WC-for-BMI residuals, physical activity tertiles, and incident cardiovascular disease.

| | Women | | | Men | | |
|---|---|---|---|---|---|---|
| **Groups** | **n total** | **n events** | **Hazard ratio (95% CI)** | **n total** | **n events** | **Hazard ratio (95% CI)** |
| **Total physical activity** | | | | | | |
| High | | | | | | |
| Low WC (reference) | 7,299 | 102 | 1.00 | 3,759 | 151 | 1.00 |
| Medium WC | 4,791 | 94 | 1.27 (0.96, 1.68) | 4,714 | 211 | 1.00 (0.81, 1.23) |
| High WC | 1,769 | 47 | 1.60 (1.13, 2.26) | 1,254 | 55 | 0.87 (0.64, 1.19) |
| Medium | | | | | | |
| Low WC | 6,599 | 143 | 1.27 (0.98, 1.63) | 3,094 | 143 | 0.98 (0.78, 1.24) |
| Medium WC | 4,853 | 121 | 1.32 (1.01, 1.72) | 4,992 | 269 | 1.04 (0.85, 1.27) |
| High WC | 2,307 | 67 | 1.41 (1.03, 1.92) | 1,777 | 108 | 1.05 (0.82, 1.35) |
| Low | | | | | | |
| Low WC | 5,415 | 161 | 1.45 (1.13, 1.87) | 2,827 | 194 | 1.25 (1.01, 1.55) |
| Medium WC | 4,430 | 176 | 1.75 (1.36, 2.24) | 5,706 | 390 | 1.12 (0.92, 1.35) |
| High WC | 2,500 | 131 | 2.13 (1.64, 2.78) | 2,744 | 232 | 1.31 (1.06, 1.62) |
| **Light intensity physical activity** | | | | | | |
| High | | | | | | |
| Low WC (reference) | 8,118 | 166 | 1.00 | 2,446 | 117 | 1.00 |
| Medium WC | 5,857 | 162 | 1.23 (0.99, 1.53) | 3,555 | 192 | 0.99 (0.79, 1.25) |
| High WC | 2,491 | 81 | 1.33 (1.02, 1.74) | 1,138 | 72 | 1.06 (0.79, 1.42) |
| Medium | | | | | | |
| Low WC | 6,729 | 144 | 1.09 (0.87, 1.36) | 3,095 | 146 | 0.96 (0.76, 1.23) |
| Medium WC | 4,873 | 133 | 1.21 (0.96, 1.52) | 4,831 | 279 | 1.01 (0.81, 1.26) |
| High WC | 2,324 | 84 | 1.45 (1.11, 1.88) | 1,763 | 130 | 1.16 (0.90, 1.49) |
| Low | | | | | | |
| Low WC | 4,466 | 96 | 1.18 (0.91, 1.52) | 4,139 | 225 | 1.14 (0.91, 1.42) |
| Medium WC | 3,344 | 96 | 1.35 (1.05, 1.74) | 7,026 | 399 | 1.04 (0.85, 1.28) |
| High WC | 1,761 | 80 | 1.82 (1.39, 2.39) | 2,874 | 193 | 1.09 (0.86, 1.37) |

| | | | | | | |
|---|---|---|---|---|---|---|
| **Moderate-to-vigorous intensity physical activity** | | | | | | |
| High | | | | | | |
| Low WC (reference) | 5,224 | 79 | 1.00 | 4,597 | 192 | 1.00 |
| Medium WC | 3,590 | 72 | 1.18 (0.86, 1.63) | 6,639 | 341 | 1.09 (0.92, 1.30) |
| High WC | 1,411 | 38 | 1.42 (0.96, 2.09) | 2,118 | 103 | 0.93 (0.73, 1.18) |
| Medium | | | | | | |
| Low WC | 6,632 | 128 | 1.13 (0.85, 1.50) | 3,000 | 166 | 1.29 (1.05, 1.59) |
| Medium WC | 4,948 | 128 | 1.34 (1.01, 1.78) | 4,976 | 259 | 1.07 (0.89, 1.29) |
| High WC | 2,176 | 66 | 1.46 (1.05, 2.03) | 1,896 | 147 | 1.42 (1.14, 1.76) |
| Low | | | | | | |
| Low WC | 7,457 | 199 | 1.39 (1.07, 1.81) | 2,083 | 130 | 1.38 (1.10, 1.72) |
| Medium WC | 5,536 | 191 | 1.60 (1.23, 2.09) | 3,797 | 270 | 1.33 (1.11, 1.61) |
| High WC | 2,989 | 141 | 1.99 (1.50, 2.63) | 1,761 | 145 | 1.43 (1.15, 1.78) |
| **Vigorous intensity physical activity** | | | | | | |
| High | | | | | | |
| Low WC (reference) | 6,220 | 87 | 1.00 (1.00, 1.00) | 4,657 | 188 | 1.00 (1.00, 1.00) |
| Medium WC | 3,711 | 62 | 1.08 (0.78, 1.49) | 5,924 | 237 | 0.88 (0.72, 1.06) |
| High WC | 1,273 | 34 | 1.58 (1.06, 2.35) | 1,584 | 72 | 0.89 (0.68, 1.17) |
| Medium | | | | | | |
| Low WC | 6,353 | 126 | 1.09 (0.83, 1.43) | 3,180 | 177 | 1.12 (0.91, 1.38) |
| Medium WC | 4,636 | 110 | 1.21 (0.91, 1.61) | 5,422 | 313 | 1.06 (0.88, 1.27) |
| High WC | 2,127 | 56 | 1.22 (0.87, 1.72) | 2,109 | 132 | 1.07 (0.86, 1.35) |
| Low | | | | | | |
| Low WC | 6,740 | 193 | 1.26 (0.98, 1.63) | 1,843 | 123 | 1.17 (0.93, 1.48) |
| Medium WC | 5,727 | 219 | 1.54 (1.19, 1.98) | 4,066 | 320 | 1.27 (1.05, 1.52) |
| High WC | 3,176 | 155 | 1.85 (1.41, 2.42) | 2,082 | 191 | 1.39 (1.13, 1.71) |

Results are from main model, adjusted for age (as timescale), ethnicity, education, living/not living with partner, employment, Townsend, diet quality, alcohol intake, smoking and depression.

**Supplementary Figure 5.** Sensitivity analysis of joint associations between waist circumference (WC) categories from World Health Organization's cut-offs, physical activity and incident cardiovascular disease without adjustment for the body mass index. Results are adjusted for age (as timescale), sex, ethnicity, education, living/not living with partner, employment, Townsend, diet quality, alcohol intake, smoking and depression. Ref: reference.



**Supplementary Figure 6.** Sensitivity analysis, excluding the first 5 years of follow-up, of joint associations between waist circumference (WC) categories from from World Health Organization's cut-offs, physical activity and incident cardiovascular disease. Results are from main model, adjusted for age (as timescale), sex, body mass index, ethnicity, education, living/not living with partner, employment, Townsend, diet quality, alcohol intake, smoking and depression. Ref: reference.