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Volume vs intensity of physical activity and risk of cardiovascular and non-cardiovascular chronic diseases

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Abstract

Background and aims While vigorous physical activity (VPA) is known to provide greater health benefits per unit time than moderate activity, the spectrum of these benefits across different chronic diseases and the relative importance of physical activity (PA) intensity vs volume remain unclear. This study examined associations between the proportion of VPA (%VPA) relative to total volume of PA and the incidence of multiple chronic disease outcomes.

Methods This prospective population-based cohort study included 96,408 participants (mean age 61.9 years, women: 56.3%) with device-measured data (wrist-worn accelerometers) and 375,730 participants (mean age 56.2 years, women: 52.2%) with self-reported PA data (IPAQ) from the UK Biobank. Main outcomes included incidence of eight chronic diseases: major adverse cardiovascular events (MACE), atrial fibrillation (AFib), type 2 diabetes (T2D), immune-mediated inflammatory diseases, metabolic dysfunction-associated steatotic liver disease (MASLD), chronic respiratory diseases (CRD), chronic kidney disease (CKD), and dementia, as well as all-cause mortality. Cox proportional hazards models were used to estimate adjusted hazard ratios and 95% confidence interval.

Results In the device-measured data, non-linear inverse dose–response relationships were observed between %VPA and all outcomes (all $P < .001$), and these patterns remained consistent across strata of total PA volume. In multivariable models adjusted for total PA volume, participants with >4% VPA had 29%–61% lower risks of these outcomes compared with those with 0% VPA. Joint analyses and population attributable fraction revealed distinct disease-specific patterns: immune-mediated inflammatory diseases showed very strong intensity-dependence with minimal contribution from PA volume (20.3% for intensity vs 1.0% for volume), while MACE (17.8% vs 6.0%), AFib (16.2% vs 5.0%), CRD (21.4% vs 5.6%), and dementia (32.3% vs 8.1%) demonstrated intensity predominance with modest contribution from PA volume, and T2D (26.6% vs 17.7%), MASLD (22.1% vs 16.6%),

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CKD (23.0% vs 15.3%), and all-cause mortality (31.4% vs 14.2%) showed more balanced contributions from both intensity and volume.

Conclusions A higher %VPA, independent of total activity volume, is inversely associated with eight major chronic diseases and all-cause mortality. Intensity consistently demonstrated a higher preventive potential than total PA volume. These findings support, whenever possible, prioritizing higher-intensity activities in clinical and public health interventions aimed at preventing non-communicable diseases.

Structured Graphical Abstract

Key Question

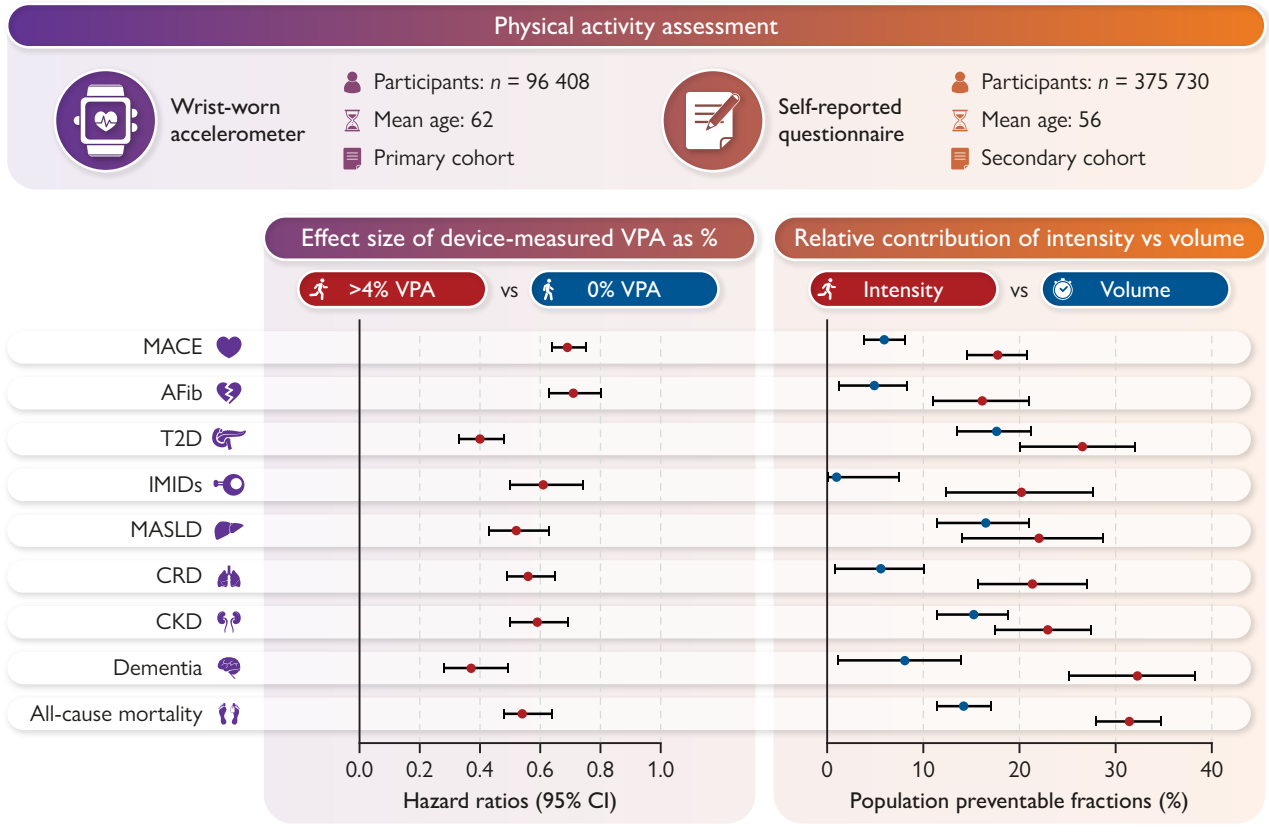
What is the spectrum of vigorous physical activity (VPA) benefits across different chronic diseases? What is the relative importance of physical activity (PA) intensity vs volume using device-based measurements?

Key Finding

A higher %VPA, independent of total activity volume, was inversely associated with eight major chronic diseases and all-cause mortality. %VPA consistently showed higher preventive potential than total PA volume across all outcomes.

Take Home Message

While meeting recommended activity volumes remains important, prioritizing PA intensity over volume may provide superior prevention benefits for most chronic diseases.



In 96 408 adults with wrist-worn accelerometer cohort (mean age 62 years), after adjustment for total PA volume, a higher proportion of VPA (>4% vs 0%) was associated with lower risks of MACE, AFib, T2D, IMIDs, MASLD, CRD, CKD, dementia, and all-cause mortality. Across all outcomes, PA intensity showed greater population preventable fractions than total PA volume, highlighting the importance of prioritizing VPA for chronic disease prevention.AFib, atrial fibrillation; CI, confidence interval; CKD, chronic kidney disease; CRD, chronic respiratory disease; IMID, immune-mediated inflammatory disease; MACE, major adverse cardiovascular event; MASLD, metabolic dysfunction-associated steatotic liver disease; PA, physical activity; VPA, vigorous physical activity.

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Keywords Physical activity • Chronic disease • Intensity • Prospective cohort study

Introduction

Physical activity (PA) is a well-established modifiable lifestyle factor that reduces the risk of numerous chronic diseases and all-cause mortality,[1] though the health effects can vary depending on the context and type of PA.[2] Both the 2020 World Health Organization PA and Sedentary Behaviour Guidelines and the PA Guidelines for Americans, 2nd Edition, recommend 150–300 min of moderate PA (MPA), 75–150 min of vigorous PA (VPA), or a combination of both per week.[3,4] These guidelines are based on the premise that, for at least some health outcomes, VPA provides greater benefits than MPA,[5] an assertion that is further supported by more recent data.[6]

Previous studies have shown that VPA leads to superior improvements in cardiorespiratory fitness, functional capacity, and several cardiometabolic risk factors compared to lower-intensity activities at equivalent volumes.[7–9] Recent findings further demonstrate that even modest amounts of VPA—as little as 15–20 min per week—are associated with substantially lower mortality risk.[10] A U.S. cohort study using self-reported data found that, for the same total volume of PA, a higher %VPA relative to total activity was associated with lower all-cause mortality.[11] A previous work study using accelerometer-based data examined brief bouts of moderate-to-vigorous intermittent lifestyle PA among adults who do not engage in structured PA and demonstrated that higher proportions of VPA (%VPA) were associated with lower major adverse cardiovascular events (MACE) and all-cause mortality risk in an inverse linear direction.[12] Notably, short bouts (<1 min) were associated with lower MACE risk only when bouts were comprised of at least 15% vigorous activity.[12] It demonstrated that %VPA may be associated with health benefits even when PA occurs in brief, incidental bouts rather than structured PA sessions.

This intensity–benefit relationship has important public health implications, particularly regarding the potential to optimize the cost-effectiveness of PA interventions—a critical consideration given that time constraints remain a primary barrier to PA adherence. However, key knowledge gaps remain regarding whether these intensity-specific benefits extend to chronic diseases beyond cardiovascular outcomes, and the relative importance of exercise intensity vs total volume across different chronic diseases.[13,14]

To fill these gaps, we utilized accelerometer-measured PA data from the UK Biobank to investigate the associations of %VPA with eight major chronic diseases—MACE, atrial fibrillation (AFib), type 2 diabetes (T2D), immune-mediated inflammatory diseases (IMIDs), metabolic dysfunction-associated steatotic liver disease (MASLD), chronic respiratory diseases (CRD), chronic kidney disease (CKD), and dementia—as well as all-cause mortality. We specifically examined the relative contributions of PA intensity vs total volume across these different chronic diseases. These eight chronic diseases were selected as they represent the major categories of non-communicable diseases that collectively account for the leading causes of major global health burdens.[15]

Methods

Data sources

The UK Biobank is a large-scale, prospective cohort study that recruited over 500,000 individuals aged 40–69 years from the general UK population between 2006 and 2010.[16] Ethical approval was granted by the North West Multicenter Research Ethics Committee (reference: 11/NW/0382), and all participants provided written informed consent. The present study was conducted using data from the UK Biobank under approved application number 90923.

Device-measured physical activity

Between 2013 and 2015, a random subset of 103,619 UK Biobank participants was given to wear an Axivity AX3 wrist-worn accelerometer (Newcastle upon Tyne, UK) on their dominant wrist continuously for 7 days, when the sensor captured the acceleration at 100 Hz with a dynamic range of ±8 g (unit of gravity).[17] The Euclidean Norm Minus One in milligravity was used to quantify the acceleration related to the movement registered. Participants were excluded if total wear time was less than 72 h or if calibration was inadequate during the monitoring period. A validated machine learning approach, combining balanced random forests with Hidden Markov models, classified 30 s epochs into movement behaviours.[17] Light, moderate, and vigorous PA were defined as 30–125 mg, >125–400 mg, and >400 mg,[18,19] respectively. Total volume of PA was quantified in metabolic equivalent minutes per week (MET-min/week), with separate estimates calculated for each intensity (light, moderate and vigorous).[20] Light MET-min/week = 3.3 × walking minutes × light days. Moderate MET-min/week = 4.0 × moderate activity minutes × moderate days. Vigorous MET-min/week = 8.0 × vigorous activity minutes × vigorous days. We calculated the %VPA to total volume of PA as following: VPA (MET-min/week) /total volume of PA (MET-min/week) × 100%.

Assessment of questionnaire-based physical activity

PA was assessed using the modified short-form International PA Questionnaire (IPAQ) in 2006–2010, which captures information on three types of activity: walking, moderate-intensity, and vigorous-intensity.[20,21] Total volume of PA was calculated as the sum of time spent in light walking, moderate, and vigorous PA, and was also additionally expressed in MET-min/week. The calculation methods for %VPA and for converting intensity minutes into PA volume (MET-min) were similar to those used in the device-based assessment.

Outcomes

The outcomes encompassed eight major chronic diseases—MACE, AFib, T2D, IMIDs, MASLD, CRD, CKD, and dementia—as well as all-cause mortality. MACE was defined as the occurrence of ST-elevation or non-ST-elevation myocardial infarction, stroke, or heart failure. Disease outcomes were classified according to the International Classification of Diseases, 10th Revision (ICD-10), with detailed definitions provided in Supplementary data online, *Table S1* and the references.[22] Mortality data, including dates and causes of death, were obtained from national death registries, while incident disease cases were identified via electronic health records from inpatient, outpatient, and primary care settings. For each disease outcome, participants with pre-existing diagnoses of that specific condition at baseline were excluded from the respective incident disease analysis. Participants with pre-existing diagnoses at baseline were excluded based on records obtained from self-report, primary care, or hospital admission sources. Person-time was calculated from the date of initial assessment (2006–2010 for questionnaire-based data; 2013–2015 for device-measured data) until the earliest occurrence of disease diagnosis, death, or the censoring date corresponding to the end of hospital record availability (November 2023).[23]

Covariates

Potential confounding variables were identified using an a priori-specified directed acyclic graph (see Supplementary data online, *Figure S1*).[24] Sociodemographic characteristics included age (in years, continuous), sex (men and women), ethnicity (white European or non-white European), educational attainment (college or university degree; A/AS levels or equivalent, O levels/GCSEs, equivalent or other professional qualifications; or none of the above), Townsend deprivation index (continuous), and assessment centers (22 categories). Lifestyle factors encompassed smoking status (never, former, or current), alcohol consumption (0 drinks per week, 1–14 drinks per week, or more than 14 drinks per week), body mass index (BMI, kg/m^2), diet score, total volume of PA (MET-min/week), and questionnaires-based sleep quality. Additional covariates included the frailty index score, blood pressure, lipid profile parameters (low-density lipoprotein cholesterol [LDL-C], high-density lipoprotein cholesterol [HDL-C], and triglycerides), estimated glomerular filtration rate (eGFR),[25] use of medications (including lipid-lowering, antihypertensive, antidiabetic, antithrombotic, and antiresorptive agents) (see Supplementary data online, *Table S2*), and intake of supplements such as vitamin D, vitamin K, and calcium. Diet scores, based on a previously validated dietary index, ranged from 0 to 10, with 1 point assigned for a healthy frequency and 0 for an unhealthy frequency of consuming fruits, vegetables, fish, processed meat, unprocessed red meat, whole grains, and refined grains (see Supplementary data online, *Table S3*).[26] Higher scores indicated better diet quality. Similarly, sleep scores (ranging from 0 to 5) were calculated using five factors: chronotype, sleep duration, insomnia, snoring, and excessive daytime sleepiness, with higher scores reflecting better sleep quality.[27] The frailty index score is based on five components—weight loss, exhaustion, weakness, low PA, and slow gait speed. The total number of criteria met determines frailty severity, yielding a score ranging from 0 to 5.[28]

Statistical analysis

Descriptive statistics were summarized as counts and proportions for categorical variables; for continuous data, means with standard deviations were reported for approximately symmetrical distributions, and medians with interquartile ranges (IQR) were used for skewed distributions. Missing covariate data were addressed using multiple imputation by chained equations with five imputations (see details in Supplementary Methods). Overall, missing data were minimal, with less than 1% missingness for most covariates (see Supplementary data online, *Table S4–S6*).

For device-based data, %VPA was categorized into four levels: No VPA (0%), >0% to ≤2%, >2% to ≤4%, and >4%. These cut-points were selected based on sample distribution (approximately 95% of participants had device-measured %VPA <5%) to ensure adequate sample sizes across categories. For questionnaire-based PA data, %VPA was categorized into four levels: No VPA (0%), >0% to ≤25%, >25% to ≤50%, and >50%, consistent with previous epidemiological studies examining VPA proportions.[11] Using age as the timescale, multivariable Cox proportional hazards models were used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for incident chronic disease and mortality across these VPA categories. Models 1 were adjusted for total PA volume and key confounders, including sociodemographic factors (age, sex, ethnicity, education, deprivation index, assessment centres), lifestyle factors (smoking, alcohol consumption, diet score, sleep quality), with total PA volume included to isolate the specific associations of VPA intensity. Model 2 additionally adjusted for medication use, supplement intake, frailty index score, BMI, blood pressure, LDL-C, HDL-C, triglycerides, and eGFR. To minimize the risk of over-adjustment for variables that might act as mediators between %VPA and the outcomes, Model 1 was used as the primary analytic model. The proportional hazards assumption was verified using Schoenfeld residuals, with no violations observed. Spearman rank correlation analysis indicated a weak to moderate association between total PA volume and %VPA ($\rho = 0.371$ for self-reported data; $\rho = 0.225$ for device-measured data). Variance inflation factors were 1.008 and 1.076, respectively, suggesting no evidence of covariate multicollinearity.

Exploratory analyses were conducted to assess the dose–response relationships between the %VPA among participants with available wearable device-measured ($n = 96{,}408$) and self-reported ($n = 375{,}730$) PA data, and the incidence of chronic diseases and all-cause mortality. Restricted cubic splines with three knots at the 10th, 50th, and 90th percentiles were used to account for potential nonlinearity.[29] Linearity was assessed using the Wald test. Additionally, joint dose–response associations between %VPA and total PA volume (categorized into tertiles) were modelled using restricted cubic splines with knots placed at the 10th, 50th, and 90th percentiles. The reference group was defined as individuals with 0% VPA and those in the lowest tertile of total PA volume. Contour plots were constructed using Poisson regression models with 40 × 40 prediction grids to estimate adjusted incidence rates (per 10,000 person-years) across different combinations of %VPA and total PA volume. We additionally conducted joint dose–response analyses examining the associations of device-measured proportions of MPA (%MPA) relative to total PA volume and of VPA within moderate-to-vigorous PA volume with all outcomes. Contour plots were also generated to illustrate disease incidence rates across combinations of %VPA and %MPA. Poisson model assumptions were verified through overdispersion testing (deviance-to-degrees-of-freedom ratios <1.5) and linearity assessments, with no evidence of assumption violations.

Population preventable fractions (PPFs) were estimated using the parametric g-formula approach to quantify the proportion of disease cases attributable to lower PA levels, assuming the entire population shifted to higher %VPA (>0% vs 0%) or higher total PA volume (middle and upper tertiles vs lowest tertile).[30–32] Individual-level predicted cumulative risks under both observed (actual) and counterfactual exposure scenarios were obtained from adjusted Cox regression models. PPFs were then calculated as $(\text{Risk}_{\text{actual}} - \text{Risk}_{\text{counteractual}})/\text{Risk}_{\text{actual}}$.[32] The 95% CIs were estimated using bootstrap resampling ($n = 500$).

Adjusted survival curves derived from the Cox models were plotted to illustrate cumulative risk across %VPA categories. Crude and standardized incidence rates (per 10 000 person-years) were calculated using Poisson regression modelling across the %VPA groups. The standardized differences and ratios between these incidence rates were determined using g-computation methods with standard parametric regression models.[33] The 95% CI for standardized incidence rate ratios and incidence rate differences were calculated using non-parametric bootstrap resampling with 500 iterations. We applied Fine and Gray competing risk regression models to calculate the 3-, 4-, and 5-year absolute risks across categories of device-measured %VPA. We assessed the Fine–Gray model assumptions by examining cumulative incidence curves to evaluate proportional hazards and by conducting likelihood ratio tests to assess linearity for continuous predictors. No violations were detected.

We performed stratified analyses by age, sex, smoking status, BMI, alcohol consumption, diet score, questionnaire-based sleep quality, and frailty index score to evaluate the consistency of associations across population subgroups. Likelihood ratio tests were used as exploratory screening tools to identify potential heterogeneity. These analyses were intended to assess the robustness of the findings rather than to formally quantify interaction effects.

To ensure the robustness of results, we implemented several sensitivity analyses: (i) excluding cases diagnosed within the first 5 years of follow-up to address potential reverse causality;[34] (ii) adjusting for baseline prevalence of the other six conditions when analysing each individual disease (e.g. when analysing T2D, we adjusted for baseline MACE, IMIDs, MASLD, CRD, CKD, and dementia; when analysing MACE, we did not adjust for AFib as it is a component of the MACE composite endpoint); (iii) adjusted for body height when examining CRD outcomes, as height is a potential risk factor for respiratory disease; (iv) restricting analyses to participants with complete covariate data; (v) excluded participants with a high frailty index score (≥3 of 5); (vi) VPA and non-VPA were examined as separate independent variables instead of the %VPA; vii7) VPA and total volume of PA were also examined using minutes of activity instead of MET-min to calculate the %VPA; (viii) replacing MET-weighting with PA energy expenditure when calculating % VPA;[19] (ix) second-order terms for age were examined to assess potential non-linear confounding; and (x) Fine and Gray competing risks regression was utilized, with death from other causes treated as a competing event. All analysis were performed using R v4.3.0, with statistical significance determined at a Benjamini–Hochberg false discovery rate of 0.05. This study adhered to STROBE guideline for cohort studies.

Results

Among the 96 408 participants with device-measured PA, 56.3% were women, with a mean age of 61.9 ± 7.9 years. Over a median follow-up of 8.8–8.9 years (varying by outcome), we observed 9366 cases of MACE, 4123 AFib, 2210 T2D, 1721 IMIDs, 1706 cases of MASLD, 2873 CRD, 2565 CKD, 942 dementia cases, and 4129 deaths (*Table 1* and Supplementary data online, *Figure S2*).

Among the 375,730 participants with questionnaire-based PA, 52.2% were women, with a mean age of 56.2 ± 8.1 years. During a follow-up period of 14.4–14.6 years, there were 58,644 cases of MACE, 25,103 AFib, 22,442 T2D, 13,163 IMIDs, 10,747 MASLD, 20,173 CRD, 17,061 CKD, 7290 dementia cases, and 30,335 deaths were recorded (see Supplementary data online, *Table S7*).

Overall, participants with higher %VPA were generally younger, more likely to be men, better educated, smoked less, and had lower obesity rates.

Associations of %VPA with disease outcomes and all-cause mortality

In device-measured PA data, compared with no VPA (0%), participants with >4% VPA had significantly lower risks of multiple outcomes in Model 1: 31% for MACE, 29% for AFib, 60% for T2D, 39% for IMIDs, 48% for MASLD, 44% for CRD, 41% for CKD, 63% for dementia, and 46% for all-cause mortality (*Table 2*). Although the association was attenuated after further adjustment in Model 2, the inverse relationship remained statistically significant (*Table 2*). The standardized incidence rates of MACE and AFib decreased from 165.4 to 114.4 and from 62.9 to 44.5 per 1000 person-years, respectively, across increasing %VPA groups (see Supplementary data online, *Table S8*). For other outcomes, consistent lower standardized incidence rates were also observed with increasing %VPA. Higher %VPA levels were associated with lower cumulative risk across all outcomes, with the differences becoming more pronounced with advancing age (see Supplementary data online, *Figure S3*). The adjusted 3-, 4-, and 5-year risks of chronic disease outcomes are shown in Supplementary data online, *Table S9*. Higher % VPA levels were associated with lower 5-year absolute risks. For example, the 5-year risk of MACE was 10.16% in the 0% VPA group and 6.41% in the >4% VPA group, whereas the corresponding risks for AFib were 4.08% and 1.70%, respectively. Comparable associations were observed for questionnaire-based %VPA, although with a smaller magnitude of associations (see Supplementary data online, *Tables S10* and *S11*).

Joint associations of %VPA and total PA volume with disease outcomes and all-cause mortality

Dose–response analyses revealed non-linear relationships between device-measured and questionnaire-based %VPA and the incidence of chronic diseases and all-cause mortality (all $P_{\text{non-linear}} < 0.001$) (see Supplementary data online, *Figure S4-S5*). After adjusting for total PA volume, higher %VPA was consistently associated with lower risk across most outcomes in both device-measured and questionnaire-based PA data. In device-measured %VPA analyses, no plateau was observed for T2D, MASLD, CRD, and CKD. In contrast, for MACE, AFib, IMIDs, dementia, and all-cause mortality, the lower risk associated with higher %VPA plateaued at around 4%–5%, with no further reductions beyond these thresholds. Similar inverse associations were observed in questionnaire-based data, although the lower risk generally plateaued at approximately 30%–40% VPA across all outcomes and was attenuated in magnitude.

In device-measured PA data, joint dose–response curves showed significant non-linear associations between %VPA and health outcomes across all tertiles of total PA volume (all $P_{\text{non-linear}} < 0.001$) (*Figure 1*). For most outcomes, individuals in higher PA tertiles had lower risks at equivalent %VPA levels, although for IMIDs, corresponding %VPA levels showed similar associations with lower risk across PA levels. These dose–response relationships remained consistent even after additional covariate adjustment in Model 2 (see Supplementary data online, *Figure S6*). Higher %MPA to total PA volume and the proportion of VPA within MVPA volume were both inversely associated with all outcomes (see Supplementary data online, *Figures S7* and *S8*). A larger %MPA was required to observe associations comparable to those seen with a smaller %VPA (see Supplementary data online, *Figures S9*). For MACE, AFib, T2D, MASLD, CKD, and all-cause mortality, the contour lines exhibited a diagonal distribution pattern, indicating that disease risk was continuously lower with concurrent increases in both total PA volume and % VPA (*Figure 2*). Conversely, for IMIDs, CRD, and dementia, contour lines were primarily vertical, indicating that lower risk was primarily associated with higher %VPA, with limited benefit from total PA volume alone. Similar patterns were observed with questionnaire-based PA data, although with attenuated associations (see Supplementary data online, *Figure S10*).

Population preventable fractions of intensity vs total volume of physical activity

Having any VPA (compared with 0% VPA group) could potentially prevent 20.3% of IMIDs, 21.4% of CRD, and 32.3% of

Table 1 Baseline characteristics of the participants with device-based physical activity data (n = 96 408)

Variable	Proportion of VPA			
	0	>0% to ≤2%	>2% to ≤4%	>4%
Age, years, mean (SD)	65.68 (6.89)	62.63 (7.55)	60.80 (7.72)	58.36 (7.70)
Sex, *n* (%)				
Male	5238 (35.39)	15 171 (37.47)	11 661 (49.45)	10 033 (57.21)
Female	9561 (64.61)	25 320 (62.53)	11 920 (50.55)	7504 (42.79)
Ethnicity, *n* (%)				
White	14 438 (97.56)	39 327 (97.13)	22 798 (96.68)	16 856 (96.12)
Non-white	361 (2.44)	1164 (2.87)	783 (3.32)	681 (3.88)
Sleep score[a], mean (SD)	3.45 (1.03)	3.58 (1.01)	3.64 (1.00)	3.73 (0.97)
Diet score[b], mean (SD)	4.82 (1.54)	4.86 (1.50)	4.82 (1.50)	4.83 (1.49)
Townsend deprivation index, mean (SD)	−1.46 (2.96)	−1.72 (2.80)	−1.82 (2.79)	−1.83 (2.76)
Frailty index[c], mean (SD)	0.80 (0.92)	0.52 (0.73)	0.41 (0.64)	0.33 (0.57)
Education, *n* (%)				
College or university degree	6105 (41.25)	16 706 (41.26)	10 163 (43.10)	8799 (50.17)
A/AS levels or equivalent, O levels/GCSEs, equivalent or other professional qualifications	7009 (47.36)	20 092 (49.62)	11 528 (48.89)	7842 (44.72)
None of the above	1685 (11.39)	3693 (9.12)	1890 (8.01)	896 (5.11)
Smoking status, *n* (%)				
Never	7884 (53.27)	22 941 (56.66)	13 480 (57.16)	10 752 (61.31)
Past	5570 (37.64)	14 720 (36.35)	8558 (36.29)	5809 (33.12)
Current	1345 (9.09)	2830 (6.99)	1543 (6.54)	976 (5.57)
Alcohol consumption frequency, *n* (%)				
0 drink per week	4949 (33.44)	11 135 (27.50)	5423 (23.00)	3755 (21.41)
1–14 drink per week	7335 (49.56)	22 214 (54.86)	13 467 (57.11)	10 317 (58.83)
> 14 drink per week	2515 (16.99)	7142 (17.64)	4691 (19.89)	3465 (19.76)
Body mass index, kg/m^2, *n* (%)				
Underweight (<18.5)	83 (0.56)	211 (0.52)	137 (0.58)	116 (0.66)
Normal (18.5–24.9)	3986 (26.93)	15 046 (37.16)	9764 (41.41)	8607 (49.08)
Overweight (25.0–29.9)	5947 (40.19)	16 833 (41.57)	10 004 (42.42)	6929 (39.51)

Continued

Table 1 *Continued*

Variable	Proportion of VPA			
	0	>0% to ≤2%	>2% to ≤4%	>4%
Obese (≥30.0)	4783 (32.32)	8401 (20.75)	3676 (15.59)	1885 (10.75)
Diastolic blood pressure, mmHg, mean (SD)	82.77 (10.64)	81.72 (10.60)	81.46 (10.58)	80.93 (10.46)
Systolic blood pressure, mmHg, mean (SD)	142.05 (19.80)	138.90 (19.38)	137.69 (19.05)	136.01 (18.34)
HDL, mmol/L, mean (SD)	1.45 (0.39)	1.49 (0.39)	1.48 (0.38)	1.49 (0.38)
LDL direct, mmol/L, mean (SD)	3.56 (0.90)	3.59 (0.86)	3.57 (0.83)	3.50 (0.81)
Triglycerides, mmol/L, median [IQR]	1.55 [1.11-2.22]	1.43 [1.02-2.05]	1.39 [0.99-2.03]	1.28 [0.91-1.88]
eGFR, mL/min/1.73 m^2, median [IQR]	95.78 [85.10-106.34]	100.06 [89.72-109.95]	101.26 [91.06-110.92]	103.61 [93.67-112.73]
Lipid-lowering medication, *n* (%)	3175 (21.45)	5404 (13.35)	2541 (10.78)	1289 (7.35)
Antihypertensive medication, *n* (%)	4438 (29.99)	7526 (18.59)	3362 (14.26)	1683 (9.60)
Antidiabetic medication, *n* (%)	882 (5.96)	893 (2.21)	353 (1.50)	185 (1.05)
|Antithrombotic medication, *n* (%)	2969 (20.06)	5230 (12.92)	2602 (11.03)	1416 (8.07)
Antiresorptive medication, *n* (%)	357 (2.41)	663 (1.64)	231 (0.98)	105 (0.60)
Vitamin D/K supplement, *n* (%)	396 (2.68)	880 (2.17)	410 (1.74)	258 (1.47)
Calcium supplement, *n* (%)	452 (3.05)	1124 (2.78)	488 (2.07)	304 (1.73)
MPA (MET-min/week), median [IQR]	927.36 [604.80–1290.24]	1733.76 [1290.24–2257.92]	2096.64 [1612.80–2741.76]	2378.88 [1814.40–3024.00]
VPA (MET-min/week), median [IQR]	0.00 [0.00–0.00]	80.64 [80.64–161.28]	241.92 [161.28–322.56]	645.12 [483.84–887.04]
LPA (MET-min/week), median [IQR]	5655.88 [4302.03–7146.77]	7268.85 [5929.97–8844.90]	6938.87 [5542.45–8605.06]	6518.08 [5207.81–8063.19]
Total volume of physical activity (MET-min/week), median [IQR]	6675.37 [5136.15–8328.14]	9165.71 [7579.09–10,994.87]	9462.01 [7507.58–11,492.84]	9716.31 [7859.51–11,750.24]

eGFR, estimated glomerular filtration rate; HDL, high-density lipoprotein; IQR, interquartile range; LDL, low-density lipoprotein; LPA, light physical activity; MET, metabolic equivalent of task; MPA, moderate physical activity; SD, standard deviation; VPA, vigorous physical activity.

[a]Sleep scores were calculated using five factors: chronotype, sleep duration, insomnia, snoring, and excessive daytime sleepiness.

[b]Health diet score was calculated based on self-reported servings of fruits, vegetables, whole grains, vegetable oil, fish, dairy, refined grains, unprocessed meats, processed meats and sugar-sweetened beverages. More details can be found in Online Supplementary data online, Table S3.

[c]Frailty index was calculated using five factors: self-reported physical activity, walking speed, weight loss, exhaustion, and grip strength.

Table 2 Associations of the proportion of device-based vigorous physical activity with risks of major chronic diseases and all-cause mortality (*N* = 96 408)

Device-based proportion of VPA (%)	Event, *n*	Crude HR (95% CI)	P_{FDR}	Model 1		Model 2	
				HR (95% CI)	P_{FDR}	HR (95% CI)	P_{FDR}
MACE							
0%	2035/12,233	1.00 (ref.)		1.00 (ref.)		1.00 (ref.)	
>0% to ≤2%	4005/36,100	0.637 (0.604–0.672)	<.001	0.821 (0.775–0.869)	<.001	0.874 (0.825–0.926)	<.001
>2% to ≤4%	2074/21,414	0.550 (0.517–0.584)	<.001	0.756 (0.707–0.809)	<.001	0.834 (0.779–0.892)	<.001
>4%	1252/16,316	0.430 (0.401–0.462)	<.001	0.692 (0.640–0.748)	<.001	0.785 (0.725–0.850)	<.001
AFib							
0%	954/14,028					1.00 (ref.)	
>0% to ≤2%	1801/39,331	0.650 (0.601–0.704)	<.001	0.861 (0.791–0.938)	.002	0.938 (0.861–1.022)	.230
>2% to ≤4%	862/22,972	0.528 (0.481–0.579)	<.001	0.752 (0.680–0.832)	<.001	0.860 (0.776–0.953)	.009
>4%	506/17,227	0.410 (0.368–0.457)	<.001	0.708 (0.629–0.798)	<.001	0.833 (0.737–0.940)	.008
T2D							
0%	554/13,273	1.00 (ref.)		1.00 (ref.)		1.00 (ref.)	
>0% to ≤2%	1029/38,634	0.620 (0.559–0.687)	<.001	0.848 (0.758–0.950)	.005	0.975 (0.870–1.092)	.710
>2% to ≤4%	430/22,834	0.434 (0.383–0.493)	<.001	0.600 (0.523–0.689)	<.001	0.783 (0.681–0.900)	.001
>4%	197/17,159	0.263 (0.224–0.310)	<.001	0.398 (0.334–0.476)	<.001	0.605 (0.506–0.724)	<.001
IMIDs							
0%	395/13,432	1.00 (ref.)		1.00 (ref.)		1.00 (ref.)	
>0% to ≤2%	769/37,965	0.673 (0.596–0.760)	<.001	0.807 (0.708–0.921)	.002	0.864 (0.756–0.987)	.083
>2% to ≤4%	361/22,376	0.533 (0.462–0.615)	<.001	0.719 (0.615–0.842)	<.001	0.795 (0.677–0.932)	.015
>4%	196/16,762	0.385 (0.324–0.457)	<.001	0.609 (0.504–0.737)	<.001	0.687 (0.566–0.834)	.001
MASLD							
0%	417/14,494	1.00 (ref.)		1.00 (ref.)		1.00 (ref.)	
>0% to ≤2%	745/39,972	0.628 (0.557–0.708)	<.001	0.824 (0.722–0.939)	.004	0.918 (0.805–1.048)	.290
>2% to ≤4%	365/23,351	0.523 (0.455–0.602)	<.001	0.722 (0.618–0.843)	<.001	0.867 (0.741–1.016)	.110
>4%	179/17,399	0.342 (0.287–0.408)	<.001	0.522 (0.430–0.633)	<.001	0.676 (0.555–0.823)	<.001
CRD							
0%	692/12,120	1.00 (ref.)		1.00 (ref.)		1.00 (ref.)	
>0% to ≤2%	1270/34,313	0.629 (0.573–0.690)	<.001	0.790 (0.715–0.874)	<.001	0.849 (0.767–0.940)	.004
>2% to ≤4%	603/20,256	0.502 (0.450–0.560)	<.001	0.698 (0.619–0.787)	<.001	0.774 (0.685–0.875)	<.001
>4%	308/15,145	0.340 (0.298–0.389)	<.001	0.564 (0.486–0.654)	<.001	0.636 (0.547–0.740)	<.001
CKD							
0%	749/14,286	1.00 (ref.)		1.00 (ref.)		1.00 (ref.)	
>0% to ≤2%	1094/39,714	0.507 (0.462–0.556)	<.001	0.826 (0.745–0.914)	<.001	0.955 (0.861–1.060)	.500
>2% to ≤4%	495/23,216	0.389 (0.347–0.435)	<.001	0.740 (0.653–0.838)	<.001	0.922 (0.811–1.048)	.320
>4%	227/17,361	0.237 (0.204–0.275)	<.001	0.586 (0.498–0.689)	<.001	0.757 (0.642–0.893)	.003
Dementia							
0%	331/14,761	1.00 (ref.)		1.00 (ref.)		1.00 (ref.)	
>0% to ≤2%	390/40,440	0.414 (0.357–0.479)	<.001	0.626 (0.533–0.736)	<.001	0.661 (0.561–0.779)	<.001

Continued

Table 2 *Continued*

Device-based proportion of VPA (%)	Event, *n*	Crude HR (95% CI)	P_{FDR}	Model 1		Model 2	
				HR (95% CI)	P_{FDR}	HR (95% CI)	P_{FDR}
>2% to ≤4%	159/23,557	0.287 (0.238–0.347)	<.001	0.519 (0.422–0.639)	<.001	0.558 (0.452–0.689)	<.001
>4%	62/17,523	0.150 (0.114–0.196)	<.001	0.368 (0.275–0.493)	<.001	0.397 (0.295-0.533)	<.001
All-cause mortality							
0%	1344/14,799	1.00 (ref.)		1.00 (ref.)		1.00 (ref.)	
>0% to ≤2%	1650/40,491	0.435 (0.405–0.468)	<.001	0.681 (0.629–0.737)	<.001	0.728 (0.671–0.789)	<.001
>2% to ≤4%	724/23,581	0.326 (0.298–0.357)	<.001	0.564 (0.511–0.623)	<.001	0.619 (0.560–0.685)	<.001
>4%	411/17,537	0.248 (0.222–0.277)	<.001	0.537 (0.476–0.607)	<.001	0.603 (0.533–0.683)	<.001

AFib, atrial fibrillation; CI, confidence interval; CRD, chronic respiratory disease; CKD, chronic kidney disease; HR, hazard ratio; IMID, immune-mediated inflammatory disease; MACE, major adverse cardiovascular event; MASLD, metabolic dysfunction-associated steatotic liver disease; T2D, type 2 diabetes; VPA, vigorous physical activity.
The analyses were all based on multivariate Cox proportional hazards models adjusted for age as the underlying timescale. Model 1: Adjustments were made for age (at the time of accelerometer assessment), sex, ethnicity, educational attainment, assessment centres, Townsend deprivation index, smoking status, alcohol consumption, diet score, questionnaire-based sleep quality, and device-based total volume of physical activity. Model 2: adjusted for variables in Model 1 + lipid-lowering medication, antihypertensive medication, antidiabetic medication, antithrombotic medication, antiresorptive medication, vitamin D supplement, vitamin K supplement, calcium supplement, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, Triglycerides, estimated glomerular filtration rate, blood pressure, body mass index, and frailty index.
P_{FDR}: The two-sided *P*-values were adjusted for multiple comparisons using the false discovery rate (FDR) method. P_{FDR} <.05 was considered statistically significant.

dementia cases, whereas total PA volume (compared with the first tertile group) showed a much lower preventive potential—only 1.0%, 5.6%, and 8.1%, respectively (*Figure 3*). In addition, for MACE, AFib, and all-cause mortality, the lower risk was also primarily associated with %VPA—for example, 17.8% vs 6.0% for MACE, 16.2% vs 5.0% for AFib, and 31.4% vs 14.2% for all-cause mortality. In contrast, for metabolism-related conditions such as T2D, MASLD, and CKD, the lower risk was associated with both total PA volume and %VPA.

Subgroup and sensitivity analyses

Consistent inverse associations between %VPA and chronic disease risk as well as all-cause mortality were observed across diverse subgroups, encompassing age categories (<60 and ≥60 years), sex (men and women), smoking history (never, current, or former), weekly alcohol consumption (0, 1–14, 14+ drinks), dietary score (<3 and ≥3), sleep score (<3 and ≥3), BMI (<30 and ≥30 kg/m^2), and frailty index (<2 and ≥2) (see Supplementary data online, *Figures S11*).

The main findings remained robust across multiple sensitivity analyses: (i) excluding incident cases within 5 years of follow-up (see Supplementary data online, *Table S12*); (ii) adjusting for baseline comorbidities for all outcomes (see Supplementary data online, *Table S13*); (iii) adjusting for body height for CRD (see Supplementary data online, *Table S14*); (iv) restricting to participants with complete covariates (see Supplementary data online, *Table S15*); (v) excluding those with high frailty index (≥3 of 5) (see Supplementary data online, *Table S16*); (vi) examining VPA and non-VPA as separate variables (see Supplementary data online, *Table S17*); (vii) using activity minutes instead of MET-minutes to calculate %VPA (see Supplementary data online, *Table S18*); (viii) replacing MET-weighting with physical activity energy expenditure when calculating %VPA (see Supplementary data online, *Table S19*); (ix) including second-order terms for age to assess non-linear confounding (see Supplementary data online, *Table S20*); and (x) applying Fine and Gray competing risks regression with death from other causes as a competing event (see Supplementary data online, *Table S21*).

Discussion

In this UK Biobank-based study, we found that, for the same total PA volume, a higher %VPA was associated with lower risks of multiple chronic diseases and all-cause mortality. In the device-measured PA data, the joint dose–response curves showed a non-linear inverse association between %VPA and health outcomes across all tertiles of total PA volume. PPF analysis revealed that %VPA consistently showed higher preventive potential than total PA volume across all outcomes. IMIDs showed very strong intensity-dependence with minimal contribution from PA volume, while MACE, AFib, CRD, and dementia demonstrated intensity predominance with modest volume contributions, and T2D, MASLD, and CKD showed more balanced contributions from both intensity and volume (*Structured Graphical Abstract*).

Our findings build upon previous evidence regarding the intensity-specific benefits of PA. While earlier studies have demonstrated that a higher %VPA is associated with reduced risks of all-cause, cardiovascular disease, and cancer mortality, our results suggest that these benefits extend to a broader spectrum of chronic diseases.[5,10,11] We observed consistent non-linear inverse associations between %VPA and multiple chronic diseases. For most outcomes, questionnaire-derived data show that inverse associations increase with higher %VPA, but tends to plateau after exceeding approximately 40%. Our device-

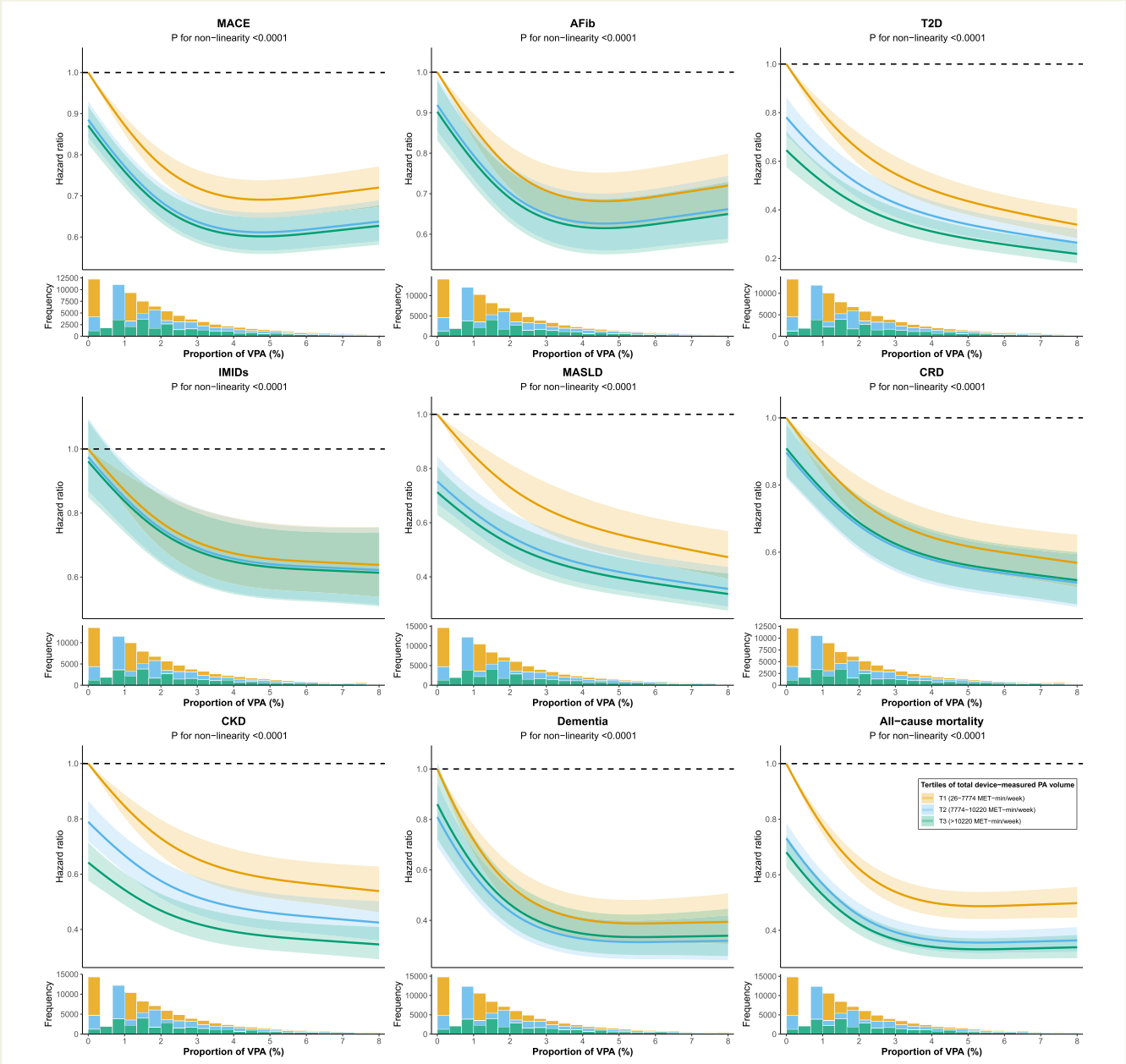

Figure 1 Joint dose–response associations between the proportion of device-measured vigorous physical activity and total physical activity volume with major chronic diseases and all-cause mortality. Restricted cubic spline curves showing the hazard ratios for eight clinical outcomes across different proportions of vigorous physical activity (%VPA, *x*-axis) stratified by tertiles of device-based total physical activity volume. The curves represent: T1 (lowest tertile, yellow), T2 (middle tertile, blue), and T3 (highest tertile, green) of total physical activity volume. The reference group consists of individuals with 0% VPA in the lowest tertile of total PA volume. Shaded areas represent 95% confidence intervals. Lower panels show the distribution of participants across %VPA categories for each tertile. The analyses were all based on multivariable Cox proportional hazards models adjusted for age as the underlying timescale. Adjustments were made for age (at the time of accelerometer assessment), sex, ethnicity, educational attainment, Townsend deprivation index, smoking status, assessment centres, alcohol consumption, diet score, and questionnaires-based sleep quality. AFib, atrial fibrillation; CI, confidence interval; CRD, chronic respiratory disease; CKD, chronic kidney disease; HR, hazard ratio; IMID, immune-mediated inflammatory disease; MACE, major adverse cardiovascular event; MASLD, metabolic dysfunction-associated steatotic liver disease; PA, physical activity; T2D, type 2 diabetes; VPA, vigorous physical activity

based findings suggest that for outcomes such as MACE, AFib, IMIDs, dementia, and all-cause mortality, the protective association of %VPA tends to plateau after exceeding approximately 5%—a threshold that already confers greater associations than the ~40% VPA observed in the questionnaire-based data. This discrepancy reflects the substantial measurement error inherent

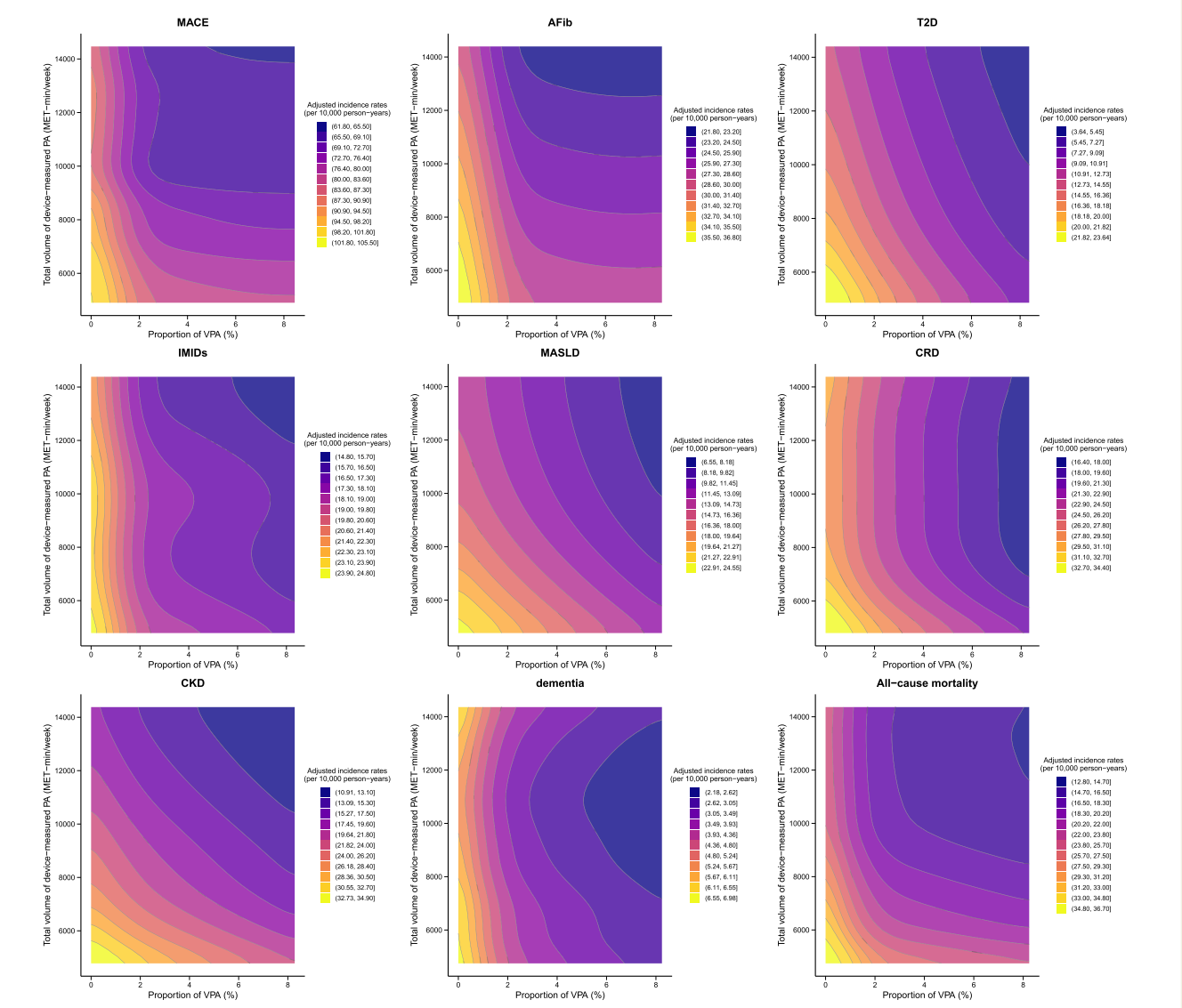

Figure 2 Contour plots of disease incidence rates across combinations of device-measured vigorous physical activity proportion and total physical activity volume. Contour plots displaying adjusted incidence rates (per 10 000 person-years) for eight clinical outcomes across different combinations of proportion of vigorous physical activity (%VPA, *x*-axis) and total volume of physical activity (MET-minutes/week, *y*-axis). Each plot was constructed using Poisson regression models with 40 × 40 prediction grids. Colour gradients represent incidence rate levels, with darker blue indicating lower rates and yellow indicating higher rates. Adjustments were made for age (at the time of accelerometer assessment), sex, ethnicity, educational attainment, Townsend deprivation index, smoking status, assessment centres, alcohol consumption, diet score, and questionnaire-based sleep quality. AFib, atrial fibrillation; CI, confidence interval; CRD, chronic respiratory disease; CKD, chronic kidney disease; HR, hazard ratio; IMID, immune-mediated inflammatory disease; MACE, major adverse cardiovascular events; MASLD, metabolic dysfunction-associated steatotic liver disease; PA, physical activity; T2D, type 2 diabetes; VPA, vigorous physical activity

in self-reported VPA data, which captures perceived blocks of leisure-time exercise during which participants believe they performed VPA rather than actual vigorous activity time, thereby diluting the true dose–response associations.[35] The device-based findings pointed towards linear (T2D) or near-linear (MASLD, CRD, and CKD) in the inverse associations of %VPA, while self-reported data failed to reveal these linear relationships. These favourable associations appear stronger when derived from device-based measurements compared to self-reported questionnaire data. The superior performance of device-based measurements can be attributed to several factors. Self-reported assessments systematically over-estimate VPA during leisure-time exercise and underestimate the large volume of brief light and moderate activities (<10 min) that occur throughout daily life, such as short walks and incidental movement.[35] Since %VPA is calculated as vigorous activity divided by total PA volume, this underestimation of the denominator may artificially inflate %VPA values in questionnaire data,

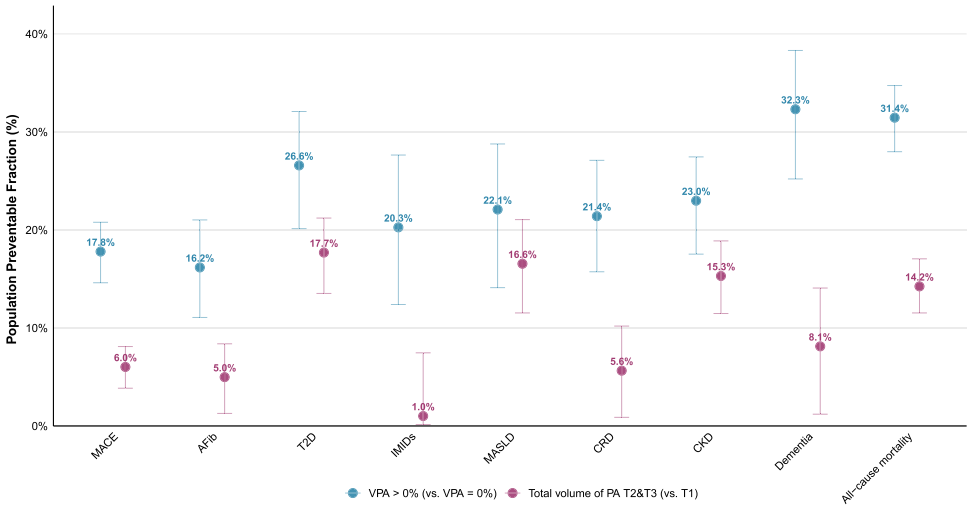

Figure 3 Population preventable fractions for proportion of device-measured vigorous physical activity and total physical activity volume across major chronic diseases and all-cause mortality. Population preventable fractions (PPFs) with 95% confidence intervals for VPA >0% (vs VPA = 0%) and total volume of PA in the middle and upper tertiles (T2&T3) vs the lowest tertile (T1) across eight health outcomes in the device-measured participants (*n* = 96,408). The analyses were all based on multivariable Cox proportional hazards models adjusted for age as the underlying timescale. Adjustments were made for age (at the time of accelerometer assessment), sex, ethnicity, educational attainment, Townsend deprivation index, smoking status, assessment centres, alcohol consumption, diet score, and questionnaire-based sleep quality. PPFs represent the estimated proportion of disease cases that could theoretically be prevented if the entire population adopted the specified physical activity levels. Total PA volume tertiles were defined as: T1 (26–7774 MET-min/week), T2 (7774–10,220 MET-min/week), and T3 (>10,220 MET-min/week). Error bars indicate 95% confidence intervals calculated using the delta method. AFib, Atrial fibrillation; CRD, Chronic respiratory disease; CKD, Chronic kidney disease; HR, Hazard ratio; IMID, Immune-mediated inflammatory disease; MACE, Major adverse cardiovascular event; MASLD, Metabolic dysfunction-associated steatotic liver disease; MET, metabolic equivalent of task; PA, physical activity; T2D, type 2 diabetes; VPA, vigorous physical activity

potentially attenuating true dose-response relationships. Additionally, device-based measurements mitigate misclassification bias, capture brief vigorous activities that may be overlooked, and provide objective intensity thresholds.

The diagonal patterns in the contour plots (where lower incidence rates were observed along both increasing %VPA and total PA volume axes) for metabolism-related conditions (T2D, MASLD, CKD) and all-cause mortality suggest that both PA volume and intensity were associated with lower risks, with patterns consistent with cumulative associations of enhanced energy expenditure and improved metabolic efficiency that correlated with both volume and intensity. In contrast, the horizontal patterns (where lower risks were observed primarily along the %VPA axis with minimal change across PA volume levels) for IMIDs (including rheumatoid arthritis, systemic lupus erythematosus, psoriasis, and inflammatory bowel diseases), CRD (chronic obstructive pulmonary disease, asthma, bronchiectasis), and dementia indicate that PA intensity—rather than total volume—may be the primary driver of the associations. PPF analysis further supported these findings. IMIDs showed the most pronounced intensity-dependence, with %VPA demonstrating over 20-fold higher PPF than total PA volume (20.3% vs 1.0%). A second tier of conditions—including MACE, AFib, CRD, and dementia—showed strong intensity-predominance, with %VPA providing 2-4 times greater PPF than total volume. In contrast, metabolism-related conditions (T2D, MASLD, CKD) demonstrated more balanced contributions, with intensity and volume showing comparable PPF (ratios of 1.3–1.5). These observations are reinforced by recent evidence indicating that 1 min of VPA yields health benefits comparable to 4–9 min of MPA or 53–156 min of LPA, while also recognizing that even very high amounts of daily LPA cannot replicate the benefits achieved through moderate or vigorous activity.[6]

VPA may uniquely trigger specific biological responses critical for these disease pathways. For IMIDs, which showed the most extreme intensity-dependence, only high-intensity activity appears capable of sufficiently modulating the complex cytokine networks and inflammatory cascades that drive disease pathogenesis.[36]

The second tier of conditions—CRD, dementia, and cardiovascular diseases—demonstrates strong but less extreme intensity-predominance, suggesting that while these conditions benefit substantially from intensity, some of the benefits may can still be achieved through volume. For respiratory conditions, vigorous activity provides superior stimulation of respiratory muscle adaptations and anti-inflammatory airway responses.[37,38] Neurological protection follows a similar pattern, where intensity-dependent neuroplasticity mechanisms, release of brain-derived neurotrophic factor, and cerebrovascular function show clear intensity thresholds but retain some volume-dependent benefits.[39,40]

VPA promotes superior improvements in endothelial function through enhanced nitric oxide bioavailability and reduced oxidative stress.[41,42] The intensity-dependent release of cardioprotective factors including atrial natriuretic peptide and anti-inflammatory adipokines may also contribute to the superior cardiovascular benefits observed with higher %VPA.[43] Previous studies have reported conflicting associations between vigorous exercise and AFib risk, with some research suggesting that extremely high volumes of endurance exercise, particularly among elite athletes, may actually increase AFib risk.[44] This paradox has been attributed to exercise-induced atrial remodelling, increased vagal tone, and structural cardiac changes observed in athletes who engage in very high volumes of training.[45] Our study extends prior work and provides insights into this apparent contradiction. Specifically, our population consisted of middle-aged and older adults from the general population rather than athletes, and the levels of vigorous activity observed were relatively low. The contour plots clearly illustrate that moderate amounts of VPA are beneficial; when %VPA is below approximately 3%, the lower AFib risk appears to be primarily associated with % VPA rather than the total volume of PA.

In contrast, metabolism-related conditions showed the most balanced intensity-volume contributions, reflecting their dual responsiveness to both cumulative energy expenditure and intensity-triggered metabolic adaptations.[46] This suggests that comprehensive activity programmes incorporating both sufficient volume and intensity remain optimal for metabolic health, unlike the intensity-focused strategies that may be most effective for immune-mediated and other strongly intensity-dependent conditions.

Public health and preventive clinical care implications

From a public health perspective, our findings support the promotion of strategies focused on time-efficient exercise and incidental PA that emphasize intensity rather than just duration, as our analyses demonstrated that higher %VPA was associated with lower risks of major chronic diseases, independent of total activity volume.[10] Specifically, for inflammatory conditions, the lower risk showed strong intensity-dependence with %VPA, suggesting that prioritizing PA intensity may be more beneficial than increasing volume. For cardiovascular, respiratory, and neurodegenerative diseases, intensity was predominantly associated with lower risk, though total PA volume also contributed. In contrast, for metabolism-related conditions and all-cause mortality, both volume and intensity contributed comparably, suggesting comprehensive activity programmes remain optimal. Our results lend support to public health campaigns and preventive clinical interventions embracing high-intensity interval training, sprint interval training, and their incidental PA analogues such as VILPA and other incidental forms of vigorous activity,[24,47] particularly for time-constrained populations and/or populations who are not able or keen to exercise in leisure time. While meeting recommended activity volumes remains important, prioritizing intensity—even in very smaller amounts[10,12]—can provide substantial population health benefits and reduce healthcare burden across multiple chronic diseases. Importantly, this does not negate the benefits of lower-intensity PA. VPA may not be feasible for older or frail adults, for whom light-to-moderate PA, reductions in sedentary time, or increases in step counts can still confer meaningful health benefits.[48–50]

Strengths and limitations

This study has several strengths, including its large sample size, prospective study design, and assessment of multiple chronic disease outcomes. The use of device-measured PA data enhances the robustness of our findings by reducing exposure measurement error.

Nonetheless, several limitations should be acknowledged. First, despite adjusting for numerous confounders, residual confounding cannot be ruled out in observational studies. Individuals who engage in higher %VPA may differ in unmeasured health behaviors or genetic factors that influence disease risk. Additionally, measurement error in self-reported confounders such as smoking status and alcohol consumption could result in incomplete adjustment, contributing to residual confounding that may have influenced our effect estimates. Second, the accelerometer data were collected over a single 7-day period, which may not fully capture long-term habitual PA patterns. However, previous studies have demonstrated high consistency in PA measurements (intraclass correlation coefficients 0.76–0.90) across repeated assessments over periods ranging from 2 months to 4 years,[51–53] and 64.0% of participants displayed stable activity trajectories in a UK Biobank subsample with at least one repeated questionnaire-based PA measurement over 7 years.[54] Third, A median interval of 5.5 years existed between baseline covariate assessment and accelerometry, though most covariates and PA status remained relatively stable over time.[12,55] Fourth, the UK Biobank had a low response rate and comprised primarily participants of European ancestry, limiting the generalizability of results to other ethnic populations. However, UK Biobank focused analyses suggest that the associations of PA with long-term cardiovascular disease outcomes and mortality is not influenced materially by poor cohort representativeness.[56] Fifth, our cause-specific Cox approach assumes conditional exchangeability of censoring, which may not hold given potential shared pathways between physical activity and competing mortality.[57] Cause-specific and Fine–Gray models also estimate different causal estimands (direct vs total effects).[57,58] However, our competing risk sensitivity analyses using Fine–Gray models, which rely on a different set of assumptions and target a different causal estimand, yielded consistent results, supporting the robustness of our findings.[57] Sixth, as noted by Hernán,[59] HRs are conditional on remaining event-free over time and may therefore be subject to built-in selection bias, particularly over long follow-up, which should be considered when interpreting our results. Seventh, our PPF estimates rely on key assumptions that may be violated in practice. These include the assumption that other risk factors remain unaffected when PA levels change, which may not hold if increased %VPA influences other health behaviours (e.g. diet, sleep) or biomarkers that mediate disease risk. Although we adjusted for major confounders, the assumption of no unmeasured confounding necessary for unbiased PPF estimation may not be fully met. Finally, our PPF estimates reflect the maximum population health impact under a

hypothetical complete exposure shift and will overestimate the effects of realistic interventions. Generalized impact fractions, which consider partial exposure shifts, are more suitable for real-world scenarios and should be considered in future intervention and policy evaluations.[60]

Conclusion

This study demonstrates that a higher %VPA, independent of total activity volume, is inversely associated with eight major chronic diseases and all-cause mortality. Distinct disease-specific patterns emerged: cardiometabolic conditions, CRD, dementia and all-cause mortality showed associations with both the volume and intensity of PA, although intensity remained the predominant factor, whereas IMIDs showed associations primarily with activity intensity. These findings support, whenever possible, prioritizing higher-intensity activities in clinical and public health interventions aimed at preventing non-communicable diseases.

Acknowledgements

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Supplementary data

Supplementary data are available at *European Heart Journal* online.

Declarations

Disclosure of Interest

E.S. is a paid consultant and holds equity in Compliment 1, a US-based commercial entity whose products relate to physical activity for the prevention of chronic disease. The other authors declare that they have no potential conflicts of interest.

Data Availability

This research has been conducted using data from UK Biobank, a major biomedical database, https://www.ukbiobank.ac.uk/. This study was performed under UK Biobank application number 90923.

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Ethical Approval

The UK Biobank study was approved by the North West Multicentre Research Ethics Committee (16/NW/0274).

Pre-registered Clinical Trial Number

None supplied.

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