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**CLINICAL RESEARCH**
*Arrhythmia/electrophysiology*

# Association between physical activity and risk of incident arrhythmias in 402 406 individuals: evidence from the UK Biobank cohort

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**Aims** Physical activity reduces cardiovascular disease burden and mortality, although its relationship with cardiac arrhythmias is less certain. The aim of this study was to assess the association between self-reported physical activity and atrial fibrillation (AF), ventricular arrhythmias and bradyarrhythmias, across the UK Biobank cohort.

**Methods and results** We included 402 406 individuals (52.5% female), aged 40–69 years, with over 2.8 million person-years of follow-up who underwent self-reported physical activity assessment computed in metabolic equivalent-minutes per week (MET-min/wk) at baseline, detailed physical assessment and medical history evaluation. Arrhythmia episodes were diagnosed through hospital admissions and death reports. Incident AF risk was lower amongst physically active participants, with a more pronounced reduction amongst female participants [hazard ratio (HR) for 1500 vs. 0 MET-min/wk: 0.85, 95% confidence interval (CI) 0.74–0.98] than males (HR for 1500 vs. 0 MET-min/wk: 0.90, 95% CI 0.82–1.0). Similarly, we observed a significantly lower risk of ventricular arrhythmias amongst physically active participants (HR for 1500 MET-min/wk 0.78, 95% CI 0.64–0.96) that remained relatively stable over a broad range of physical activity levels between 0 and 2500 MET-min/wk. A lower AF risk amongst female participants who engaged in moderate levels of vigorous physical activity was observed (up to 2500 MET-min/wk). Vigorous physical activity was also associated with reduced ventricular arrhythmia risk. Total or vigorous physical activity was not associated with bradyarrhythmias.

**Conclusion** The risk of AF and ventricular arrhythmias is lower amongst physically active individuals. These findings provide observational support that physical activity is associated with reduced risk of atrial and ventricular arrhythmias.

**Keywords** Atrial fibrillation • Ventricular arrhythmias • Exercise • Physical activity • Bradyarrhythmias

## Introduction

Large prospective cohorts demonstrate a prevalent arrhythmia in 1% of adults aged <55 years and ~5% amongst those aged 65–73 years.[1] A large proportion of this is borne by atrial fibrillation (AF). The global burden of AF has increased progressively over the past three decades,[2] potentially due to increased longevity and greater risk factor prevalence.[3,4]

Physical activity is inversely associated with cardiovascular morbidity and mortality.[5] The incidence of ischaemic heart disease and heart failure declines progressively as physical activity volume increases.[6,7] A number of population studies have addressed whether AF

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incidence is similarly reduced amongst physically active individuals.[8] In some,[9–12] but not all,[13] studies, AF risk declines amongst those who self-report a physically active lifestyle. There is also evidence that the benefits of a physical activity lifestyle may differ between males and females.[10,11] In contrast to the potential benefits of regular physical activity, endurance sports participation paradoxically increases the risk of atrial arrhythmias.[14,15]

The apparent 'u-shaped' relationship between the volume of self-reported physical activity and arrhythmia risk has not been addressed in a single cohort. The UK Biobank is a prospective study of ~500 000 individuals with detailed assessment of baseline physical characteristics, risk factors, prevalent medical conditions, and long-term follow-up via linked medical records. Leveraging this cohort, we explored the association between baseline physical activity and incident arrhythmias, including AF, ventricular arrhythmias, and bradyarrhythmias. Accounting for potentially non-linearity in the association between activity status and incident arrhythmias, this study provides comprehensive data on whether physical activity reduces the risk of developing common cardiac arrhythmias.

# Methods

## Study design

The UK Biobank cohort includes 502 543 community-dwelling individuals, aged 40–69 years, recruited between April 2007 and December 2010. Participants were invited to attend 1 of 22 assessment centres around the UK, where they completed extensive touch screen questionnaires as well as undertaking physical measurements. In this prospective, population study, self-reported physical activity habits formed the primary exposure variable with sociodemographic factors, lifestyle habits, and comorbidities as covariates. This analysis was restricted to the 402 406 participants who completed physical activity screening at baseline. All participants were followed up for health outcomes through linkage to national electronic health-related data sets. Participants provided written informed consent to participate in research as previously described. The UK Biobank was approved by the UK Biobank Research Ethics Committee (reference number 11/NW/0382).

## Clinical characteristics

Age, sex, and anthropometric measures were attained during initial study visits. Additionally, lifestyle habits were assessed at baseline by detailed health questionnaires. Smoking status and alcohol intake were evaluated by self-report. We also reviewed prevalent clinical comorbidities by self-reported questionnaire, including hypertension, obstructive sleep apnoea, Type II diabetes, arrhythmias, heart failure, valvular disease, and coronary disease.

## Physical activity assessment

Physical activity was assessed at baseline using the self-reported short-form international physical activity questionnaire (IPAQ). The IPAQ questions participants on three types of activity (walking, moderate, and vigorous-intensity activities). From these questions, the total physical activity volume can be computed in metabolic equivalent-minutes per week (MET-min/wk). Additionally, the MET-min/wk within each type of activity (i.e. walking, moderate-intensity, and vigorous intensity) was calculated.

To assess any potential thresholds for risk, we performed analyses using physical activity dose as a continuous exposure variable. To assess the association between vigorous physical activity and arrhythmia risk, the above analysis was repeated with self-reported vigorous physical activity as a continuous exposure variable.

## Arrhythmia endpoints and follow-up

The primary endpoints were the diagnosis of atrial arrhythmias (fibrillation or flutter, grouped as AF), bradyarrhythmias and ventricular arrhythmias. Incident arrhythmias were classified by at least 1 ICD-10 code for the condition listed as either a primary diagnosis, secondary diagnosis, or cause of death for a linked medical encounter. We also used the occurrence of a relevant procedure for each arrhythmia subtype. Briefly, incident AF included hospital diagnosis or death due to AF or flutter, and operative procedures relating to AF including catheter ablation. Bradyarrhythmias included diagnosis of second-degree atrioventricular (AV) block, complete AV block, sick sinus syndrome, and operative procedures relating to bradyarrhythmias including pacemaker implantation. Ventricular arrhythmias included ventricular tachycardia, ventricular fibrillation, cardiac arrest, and catheter ablation of the ventricular wall. Supplementary material online, *Table S1* lists the rhythm abnormality definitions used in this analysis. In the analysis of AF incidence, we excluded all participants who self-reported prevalent AF at study entry. For the analysis of bradyarrhythmias and ventricular arrhythmias, we excluded all participants who reported having a cardiac implantable electronic device at baseline. Hospital admissions were identified through linkage with the Health Episode Statistics records (England and Wales) and to the Scottish Morbidity Records (Scotland). Date and cause of death were obtained from death certificates held by the National Health Service Information Centre for participants from England and Wales, and the NHS Central Register Scotland for participants in Scotland. Person-time for each participant was taken from the date of first assessment and censored at the date associated with the development of arrhythmia, date of death or last known follow-up (9 February 2016 for Wales, 16 February 2016 for England, and 31 October 2015 for Scotland), whichever occurred earliest.

## Statistical analysis

Baseline variables were reported as mean and standard deviation for normally distributed variables, median, and interquartile range (IQR) for skewed data and proportions for categorical variables. The association between baseline physical activity and arrhythmia risk was reported using baseline self-reported physical activity as a continuous exposure variable. We used Cox proportional hazards to assess the influence of association between physical activity and each arrhythmia type, independently. With physical activity as a continuous exposure variable, we used restricted cubic splines with knots placed at the 5th, 35th, 65th, and 95th percentiles to assess the potential non-linear effect of physical activity on arrhythmia incidence. We then performed general contrasts of regression coefficients for physical activity to estimate hazards for pre-defined levels of physical activity at 500, 1000, 1500, 2000, 2500, and 500 MET-min/wk with 0 MET-min/wk as the referent value. In secondary analyses, we modelled vigorous physical activity, with adjustment for non-vigorous physical activity. For each arrhythmia endpoint, we ran a multivariate-adjusted model, with adjustment for age, sex, body mass index, smoking, alcohol intake, prevalent Type 2 diabetes, hypertension, sleep apnoea, heart failure, valvular disease, and coronary heart disease. Given previous findings regarding discrepant effects of physical activity amongst males and females, we chose *a priori* to assess for potential sex-dependent effects. We first included an interaction term between physical activity and sex. If this interaction did not reach statistical significance ($P < 0.10$), the interaction term was dropped from the model. Where the interaction term was significant, we assessed the association between physical activity and incident arrhythmia, for males and females separately. We assessed the

**Table 1 Baseline characteristics and risk factors amongst UK Biobank participants who completed physical activity assessment ($n = 402\,406$)**

| Characteristic and risk factor | Female ($n = 210\,811$) | Male ($n = 191\,595$) |
|---|---|---|
| Age (years) | 56 ± 8 | 57 ± 8 |
| BMI (kg/m$^2$) | 26.9 ± 5.1 | 27.8 ± 4.2 |
| Waist circumference (cm) | 84 ± 12 | 97 ± 11 |
| Body fat (%) | 36 ± 7 | 25 ± 6 |
| Systolic BP (mmHg) | 137 ± 20 | 143 ± 18 |
| Diastolic BP (mmHg) | 81 ± 11 | 84 ± 11 |
| Smoker, *n* (%) | 18 201 (8.6) | 22 942 (12.0) |
| Daily alcohol, *n* (%) | 35 406 (16.8) | 49 852 (26.0) |
| HTN, *n* (%) | 47 940 (22.7) | 58 936 (30.8) |
| OSA, *n* (%) | 290 (0.1) | 1150 (0.6) |
| HF, *n* (%) | 211 (0.1) | 472 (0.2) |
| Type 2 DM, *n* (%) | 7476 (3.5) | 12 909 (6.7) |
| Valve disease, *n* (%) | 1833 (0.9) | 1416 (0.7) |
| CAD, *n* (%) | 4889 (2.3) | 13 531 (7.1) |
| AF, *n* (%) | 2009 (1.0) | 3632 (1.9) |
| Weekly physical activity (MET-min), median (IQR) | 1720 (792–3389) | 1824 (810–3746) |
| Weekly vigorous physical activity (MET-min), median (IQR) | 160 (0–720) | 240 (0–960) |

AF, atrial fibrillation; BMI, body mass index; BP, blood pressure; CAD, coronary artery disease; DM, diabetes mellitus; HF, heart failure; HTN, hypertension; OSA, obstructive sleep apnoea.

proportional hazards assumption by inspecting log–log plots for all endpoints. All statistical analyses were performed using R Version 3.4.0 (R Foundation for Statistical Computing, Vienna, Austria).

# Results

This cohort consisted of 402 406 individuals who had completed physical activity screening at baseline. The mean age at initial assessment was 56 ± 8 years with 52.4% of the cohort being female. The baseline characteristics of the population are shown in *Table 1*. The median follow-up time was 7.0 years (IQR: 6.3–7.7). The distribution of total physical activity and vigorous physical activity volume for the entire cohort is shown in *Figure 1*. The median (IQR) weekly physical activity volume for the cohort was 1770 (2554) MET-min/wk. Using a lower cut-off of 500 MET-min/wk to reflect the lower range of guideline-recommended physical activity, 63 479 (15.8%) individuals were insufficiently active. Furthermore, 164 838 (41.0%) individuals reported no participation in vigorous physical activity.

## Atrial fibrillation/flutter

After exclusion of participants with prevalent AF, there were 8640 incident AF events across 2 763 534 person-years of follow-up (Incident rate 3.13 events per 1000 person-years, 95% CI: 3.06–3.19). Total physical activity dose was modestly associated with reduced incident AF ($\chi^2 = 23.1$, $P < 0.001$). We observed evidence of an interaction between sex and total physical activity ($\chi^2 = 11.4$, $P = 0.010$). There was a stronger association between physical activity and incident AF amongst females ($\chi^2 = 13.0$, $P = 0.005$), than for males ($\chi^2 = 9.0$, $P = 0.029$). Inspection of the plot and regression coefficient contrasts (*Figure 2*, Supplementary material online, *Table S2*) between physical activity and incident AF for males, revealed evidence of reduced AF incidence from 500 (HR 0.95, 95% CI 0.91–1.0) to 1500 MET-minutes/wk (HR 0.90, 95% CI 0.82–1.0). In contrast, amongst females, physical activity was associated with reduced incident AF at all levels from 500 (HR 0.94, 95% CI 0.88–1.0) to 5000 MET-min/wk (HR 0.80, 95% CI 0.71–0.91).

In a secondary analysis, we explored the relationship between vigorous physical activity dose and incident AF (*Figure 2*, Supplementary material online, *Table S2*). There was a statistically significant interaction between vigorous physical activity and sex ($\chi^2 = 13.9$, $P < 0.001$), in the association with incident AF. For male participants, vigorous activity in the low to moderate range was not associated with any appreciable difference in AF incidence. However, at extreme doses of vigorous activity, there was a 12% increase in incident AF (HR at 5000 Vigorous MET-min/wk: 1.12, 95% CI 1.01–1.25). In contrast, for female participants, vigorous physical activity was associated with an 8–16% lower AF incidence between 500 (HR 0.92, 95% CI 0.87–0.97) and 2500 MET-min/wk (HR 0.84, 95% CI 0.75–0.95).

## Ventricular arrhythmias

*Figure 3* shows the association between weekly physical activity dose and incident ventricular arrhythmias. There were 1266 ventricular arrhythmia events across 2 798 630 person-years of follow-up (incident rate 0.45 events per 1000 person-years, 95% CI 0.43–0.48). We observed no evidence of an interaction between physical activity and sex on incident ventricular arrhythmias ($\chi^2 = 1.2$, $P = 0.75$). There was a modest association between physical activity dose and incident ventricular arrhythmias ($\chi^2 = 8.1$, $P = 0.23$). Weekly physical activity at all levels between 500 (HR 0.89, 95% CI 0.81–0.98) and 2500 MET-min/wk (HR 0.80, 95% CI 0.66–0.97), was associated with a reduced risk of incident ventricular arrhythmias (*Figure 3*, Supplementary material online, *Table S3*).

In secondary analyses assessing, the impact of vigorous physical activity, we found a statistically significant association with ventricular arrhythmia incidence ($\chi^2 = 7.0$, $P = 0.031$). Vigorous physical activity from 500 (HR 0.90, 95% CI 0.82–0.97) to 2500 MET-min/wk (HR 0.80, 95% CI 0.67–0.95) was associated with a reduction in ventricular arrhythmia incidence (*Figure 3*, Supplementary material online, *Table S3*).

## Bradyarrhythmias

We observed 4043 bradyarrhythmia events over 2 803 255 person-years of follow-up (Incident rate 1.44. events per 1000 person-years, 95% CI: 1.40–1.49). There was no significant interaction between total physical activity and sex on incident bradyarrhythmia risk. We did not observe any statistically significant association between total physical activity and the risk of bradyarrhythmias ($\chi^2 = 1.2$, $P = 0.76$, *Figure 4*).

There was a statistically significant association between sex and vigorous physical activity risk on incident bradyarrhythmias ($\chi^2 = 8.3$,

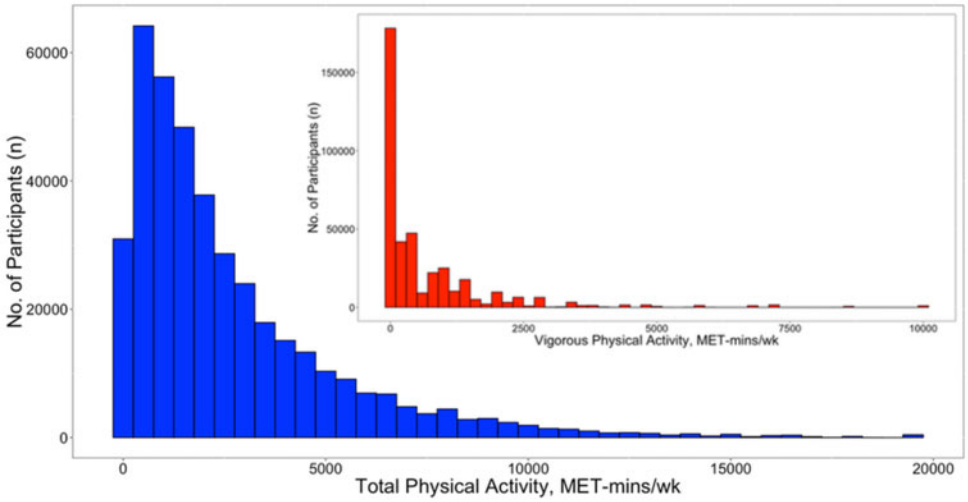



**Figure 1** Histogram of total physical activity (main, blue) and vigorous physical activity (inset, red) amongst UK Biobank participants who completed physical activity assessment.

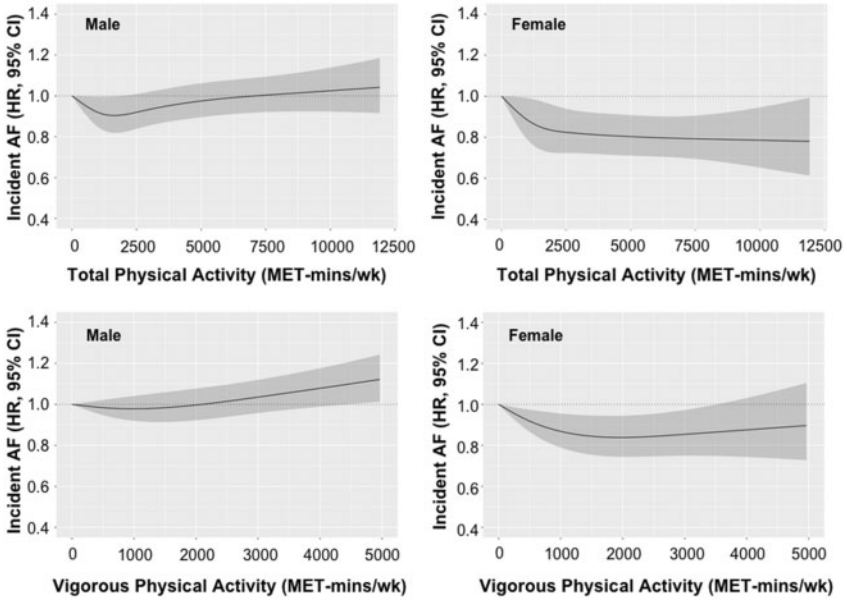



**Figure 2** Plot of incident atrial fibrillation risk against total physical activity (upper panel) and vigorous physical activity (lower panel) stratified by sex. The shaded area represents the 95% confidence bands. All models adjusted for age, body mass index, smoking, alcohol intake, hypertension, Type 2 diabetes, sleep apnoea, heart failure, valvular disease, and coronary artery disease.

$P = 0.016$). The association between vigorous physical activity and bradyarrhythmias (*Figure 4*, Supplementary material online, *Table S4*) reached statistical significance for females ($\chi^2 = 13.1$, $P = 0.001$) but not for males ($\chi^2 = 4.9$, $P = 0.085$). Amongst female participants, the reduction in bradyarrhythmia risk ranged from 9% to 18% between 500 (HR 0.91, 95% CI 0.86–0.96) and 2500 MET-min/wk (HR 0.82, 95% CI 0.73–0.91).

# Discussion

This study provides a number of notable findings on the relationship between physical activity and cardiac arrhythmias. First, achieving guideline-directed volumes of total physical activity (>500 MET-min/wk) is associated with a reduced risk of incident AF, which is more pronounced amongst females than males. Specifically, the association

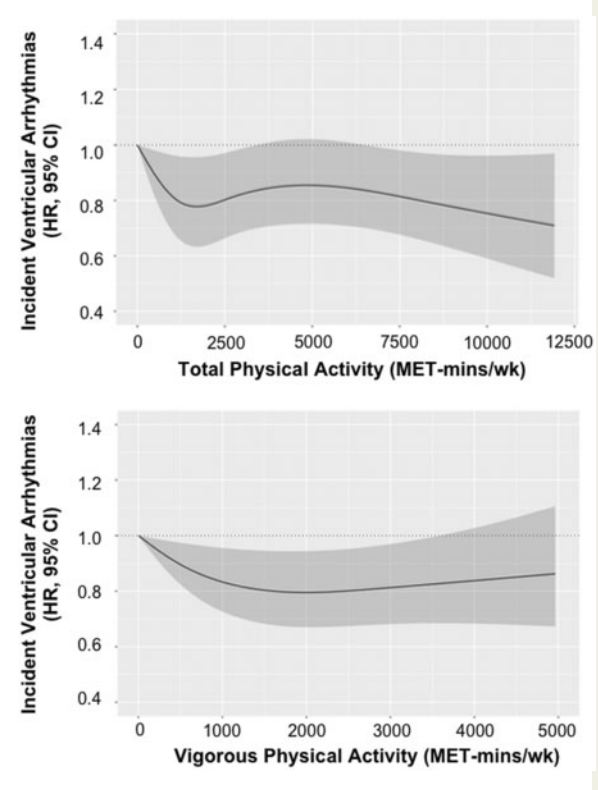



**Figure 3** Plot of incident ventricular arrhythmia risk against total physical activity (upper panel) and vigorous physical activity (lower panel). We observed no statistical interaction between physical activity and sex. Therefore, the association between physical activity and ventricular arrhythmia risk is presented for the entire cohort. The shaded area represents the 95% confidence bands. All models adjusted for age, sex, body mass index, hypertension, Type 2 diabetes, sleep apnoea, heart failure, valvular disease, and coronary artery disease.

between physical activity and incident AF declined in females up to 5000 MET-min/wk, whereas males demonstrated a modest decline in AF risk only up to 2000 MET-min/wk. Second, the incidence of ventricular arrhythmias was significantly lower amongst active individuals, up to 2500 MET-min/wk. Finally, we found no evidence supporting an association between incident bradyarrhythmia risk and physical activity.

Lifestyle-based risk factors, such as obesity, hypertension contribute to an elevation in the risk of AF.[16,17] Physical activity not only promotes risk factor control but also appears to independently reduce the development of AF. Increased physical activity was associated with a reduced risk of incident AF that was more pronounced amongst female participants. Specifically, meeting or exceeding guideline levels of physical activity in females was associated with a reduced risk of incident AF by 6–20%, consistent with that reported in previous population studies.[11] Additionally, the reduction of AF risk is consistent with data showing that elevated cardiorespiratory fitness is associated with lower AF risk.[18] Of note, we observed a modest association amongst male participants, that reached statistical significance only between 500 and 1500 MET-min/wk. Similarly, the subsequent analysis of *vigorous* physical activity revealed discrepant findings between male and female participants. Amongst males, there was no evidence of reduced AF incidence amongst participants who engaged in vigorous physical activity. Intriguingly, a high dose of vigorous physical activity was associated with a 12% increase in incident AF. In contrast, participation in vigorous physical activity over the 500–2500 MET-min/wk range was associated with an 8–16% reduction in AF risk for females, with no evidence of increased risk in the upper range of vigorous activity.

This analysis provides observational support for an increase in incident AF risk with high volumes of intensive activity, as has been observed elsewhere.[12] Given that the method of physical activity screening in this study did not specifically address endurance sports participation, we are unable to provide specific insight into the risk of AF associated with these sporting activities. However, these findings do confirm that AF risk may be raised amongst male participants of regular vigorous physical activity well above recommended guidelines levels. Future studies specifically focusing on intensive vigorous physical activity may be needed to finally answer this question and to allow clear recommendations for athletes. The mechanisms through which physical activity reduces incident atrial arrhythmias likely includes enhanced risk factor control, preserved cardiac function, and lower exposure to the potential arrhythmogenic effects of inflammation and oxidative stress.[8,19]

We also demonstrated a reduction in the risk of incident ventricular arrhythmias amongst physically active participants. Increasing levels of physical activity were associated with an 11–22% reduction in incident ventricular arrhythmia risk over the range of 500–2500 MET-min/wk. This observation is consistent with previous data amongst smaller cohorts demonstrating a reduction in sudden cardiac death for individuals with higher levels of physical activity and cardiorespiratory fitness.[20] Mechanisms such as stabilization and regression of atherosclerosis amongst participants with known or subclinical coronary disease[21] as well as the more favourable autonomic balance observed amongst active individuals[22] may contribute to the reduction of ventricular arrhythmias. Importantly, we observed a relatively stable reduction in ventricular arrhythmia risk across a broad range of total and vigorous physical activity levels.

To provide a more comprehensive analysis of the benefits of physical activity on cardiac rhythm abnormalities, we also evaluated the association between physical activity and incident bradyarrhythmias. Few studies have described whether activity or exercise habits modulate the incidence of these common arrhythmias. Our data did not provide any support for a reduction in bradyarrhythmias with higher volumes of total physical activity. Interestingly, we did find a significant association between vigorous physical activity and bradyarrhythmia risk for females, but not males. Specifically, vigorous physical activity across the range of 500–2500 MET-min/wk was associated with a 9–18% lower risk of bradyarrhythmias in female participants. To our knowledge, this is one of the first studies to describe such an association, which is worthy of further investigation. Although we have little data on the potential causal mechanisms, this data does suggest that higher physical activity may be associated with a preservation of sinus node function or conduction amongst this cohort. Importantly, we also did not find any evidence of an increase in bradyarrhythmias at the upper extremes of physical activity, despite

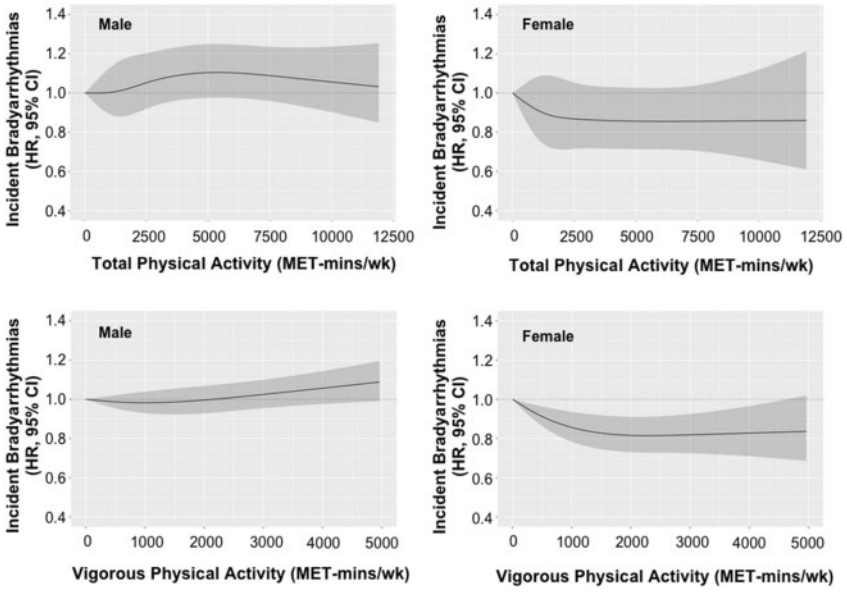
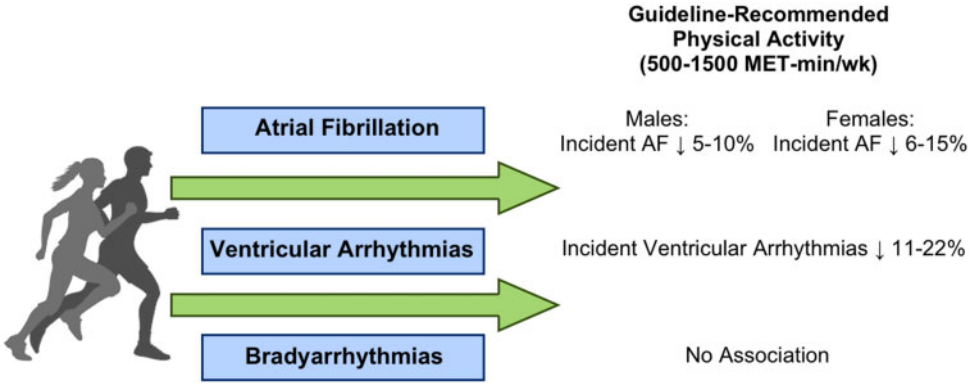



**Figure 4** Plot of incident bradyarrhythmia risk against total physical activity (upper panel) and vigorous physical activity (lower panel) stratified by sex. The shaded area represents the 95% confidence bands. All models adjusted for age, body mass index, smoking, alcohol intake, hypertension, Type 2 diabetes, sleep apnoea, heart failure, valvular disease, and coronary artery disease.




**Take home figure** Guidelines directed physical activity (5–1500 MET-min/wk) is associated with a reduction in incident atrial fibrillation from both males and females, with a largest effect for females. Similarly, physical activity is associated with a reduction in ventricular arrhythmias. However, we observed no association between physical activity and bradyarrhythmia risk.

some data suggesting that these arrhythmia types may occur more frequently amongst endurance sports participants.[15]

Collectively, these findings reinforce the importance of maintaining adequate physical activity habits to reduce cardiovascular disease burden. Cardiac rhythm abnormalities result in significant morbidity and healthcare burden.[23] It has been estimated that modifiable risk factors explain ~50% of incident AF cases.[24] Furthermore, risk factor modification, including structured exercise, has been shown to reduce the burden of arrhythmia and reverse abnormal atrial remodelling amongst patients with diagnosed AF.[25–28] Further data are needed to evaluate whether the introduction of physical activity or structured exercise programmes can offset the elevated incidence of arrhythmias in 'at-risk' individuals.

## Strengths and limitations

There are several unique strengths of this study; first, the UK Biobank is a large, prospective cohort that includes validated physical activity assessment amongst over 400 000 individuals, making this the largest analysis to date of the relationship between physical activity and cardiac arrhythmias with the inclusion of both males and females. Second, arrhythmia endpoints were collected using linkage to electronic medical records and death reports. Third, by the non-linear

analysis with physical activity modelled as a continuous exposure variable, we tested for potential benefit thresholds regarding the volume of activity, thus providing more clinically relevant information with the potential to guide future recommendations.

We acknowledge several limitations within this study. Physical activity was assessed by self-report, which may introduce some bias., the IPAQ does not specifically delineate sports-related physical activity that may have permitted closer investigation into the link between endurance sports participation and the development of cardiac arrhythmias. Physical activity status was only reported at baseline, opening the potential for time-varying changes in activity habits, which may influence subsequent arrhythmia risk. Similarly, confounding variables, such as cardiovascular risk factors and prevalent heart disease, were only assessed at baseline. We also used linked data on hospital admissions and death reports to diagnose incidence arrhythmias, which may have resulted in an underestimation of true incidence, given the potential for subclinical episodes of arrhythmias. Finally, the UK Biobank cohort is a relatively healthy cohort, demonstrating a 'healthy volunteer bias',[29] which may limit the generalizability of these findings to the broader population. Similarly, the physical activity profile of this cohort compared favourably to global and regional estimates.[30]

# Conclusions

In this comprehensive analysis of the association between physical activity and incident cardiac arrhythmias, we demonstrate that both atrial and ventricular arrhythmias are less frequent amongst physically active participants. We did not observe any association between total physical activity habits and bradyarrhythmic events, although female participants engaging in vigorous physical activity appear to carry a lower risk of developing bradyarrhythmias. Importantly, this data supports an association between higher physical activity and reduced arrhythmia risk up to 2500 MET-min/wk, which is higher than current physical activity guidelines. We also found that moderate amounts of vigorous physical activity (up to 2500 MET-min/wk) are associated with reduction in AF risk amongst females and ventricular arrhythmias across the entire cohort, independent of total activity volume. These findings suggest that low physical activity habits should be added to the list of lifestyle-based risk factors associated with the development of AF. Additional clinical intervention studies specifically focusing on intensive vigorous physical activity may be needed to allow clear recommendations for athletes and patients with AF who may wish to partake in these types of activity.

# Supplementary material

Supplementary material is available at *European Heart Journal* online.

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**Conflict of interest:** D.L. reports having served on the advisory board of Microport and Medtronic. D.L. reports having received lecture and/or consulting fees from Microport, Medtronic, Pfizer, and ResMed. D.L. reports having received research funding from Sanofi, ResMed, and Medtronic. J.M.L.H. reports that the University of Adelaide has received on his behalf lecture and/or consulting fees from Medtronic and Pfizer/BMS. D.H.L. reports that the University of Adelaide has received on his behalf lecture and/or consulting fees from Abbott Medical, Boehringer Ingelheim, Bayer, and Pfizer. P.S. reports having served on the advisory board of Boston Scientific, CathRx, Medtronic, Abbott Medical, and Pacemate. P.S. reports that the University of Adelaide has received on his behalf lecture and/or consulting fees from Medtronic, Boston Scientific, and Abbott Medical. P.S. reports that the University of Adelaide has received on his behalf research funding from Medtronic, Abbott Medical, Boston Scientific, and Microport. All other authors have no conflict of interest to declare.

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