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Impact of physical activity category on incidence of cardiovascular disease; results from the 10-year follow-up of the ATTICA Study (2002-2012)

Physical activity and CVD

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ABSTRACT
The aim of the study was to examine the effects of physical activity (PA) level on 10-year cardiovascular disease (CVD) incidence, taking into consideration several clinical and lifestyle risk factors along with the potential moderating role of gender. An analysis was undertaken on data from the ATTICA prospective cohort study (10-year follow-up, 2002-2012), which followed a Greek adult population (aged 18-89 years). A total n=317 of fatal and nonfatal CVD events occurred amongst the 2020 participants. After adjusting for the lifestyle and clinical risk factors as potential confounders, odds ratio (ORs) of CVD risk of individuals who reported being sufficiently active and highly active were decreased by 58% (95%CI: 0.30, 0.58) and 70% (95%CI: 0.15, 0.56), when compared to those who were inactive/insufficiently active, respectively. Men had nearly two-fold increase in risk of CVD (95%CI: 1.62, 2.18) versus women. Stratified analysis by gender, revealed that sufficiently active men, had 52% (95%CI: 0.24, 0.97) reduced risk of CVD incidence when compared to inactive males, while, for women, the role of PA lost significance following adjusting for lifestyle factors. The current data suggests a beneficial effect of even moderate physical activity levels on 10-year incidence of CVD, reinforcing the importance of physically activity, especially for men.
Keywords: physical activity level, CVD, prospective study

Highlights

- Moderate physical activity levels protect against CVD
- Physical activity is protective for males but not females
- Physical activity does not appear to be dose-related to CVD risk

INTRODUCTION

Despite significant efforts with respect to cardiovascular disease (CVD) prevention globally, CVD remains the major challenge to public health. It is the leading cause of death worldwide and a major cause of reduced quality of life (1). According to the 2020 goals set by the American Heart Association (AHA), to improve cardiovascular health, seven major modifiable CVD risk factors, namely physical activity (PA), blood pressure, cholesterol, body weight, dietary habits, smoking and blood glucose, need to be addressed (2). Sedentary lifestyle is a critical risk factor associated with the development of chronic diseases including CVD, obesity, diabetes mellitus and some cancers. Whilst physical activity has been recognised as an effective lifestyle approach which reduces risk of the aforementioned conditions, reversing their negative impact on metabolic abnormalities and improving health (3, 4).

The AHA and the European Society of Cardiology (ESC) recommend that all adults could improve their CVD health by engaging in either 150 min of moderate PA per week or 75 minutes of vigorous PA per week or their combination (2, 5). The 5-year follow-up of the ATTICA Study (2001-2006) revealed that almost two in three men and women in a Greek population were physically inactive or insufficiently active (6). Moreover, during the same period, the Greek population as a whole moved from a low to a moderate CVD-risk profile (6), suggesting that public health campaigns should look to better promote physical activity in order to prevent a steep increase in CVD incidence.

When considering CVD primary prevention, it has been suggested that inclusion of PA to CVD risk scores would improve the accuracy and precision of CVD risk prediction (7). Incorporating PA, into everyday screening tools, which identify high-CVD risk individuals in clinical practice should be healthcare priority as should be the promotion of PA to both patients and the general public. In a recent meta-analysis of prospective studies the authors concluded that the beneficial effect of PA category on CVD health was dose-related, however this analysis was pooled for both genders (8), despite the fact that there is discussion concerning the gender-dependent physiology of the aging heart (9). To the best of our knowledge, the prospective effect of physical activity on CVD risk, in a low to moderate CVD risk population (e.g. a Greek cohort) has not been extensively evaluated. Specifically, there is a lack of investigation into the potential moderating effects of the gender and other CVD risk factors (smoking, unhealthy diet, obesity) on the potential beneficial effects of physical activity in reducing CVD risk.

The aim of this study was to evaluate the effect of physical activity category on 10-year CVD incidence in a moderate CVD risk population, while considering the potential influencing role of gender, along with lifestyle behaviours (smoking and diet quality) and clinical risk factors (diabetes, hypertension and hypercholesterolemia).

METHODS

Baseline sampling (2001-2002)

The ATTICA is a large prospective observational cohort study, which started collecting data form CVD-free people in Greece, during 2001-2002, in the greater Athens area (78% urban and 22% rural regions). Exclusion of CVD at baseline was ensured with a detailed clinical assessment, following standard criteria, which have been presented elsewhere (10). Of the 4056 inhabitants, who were randomly invited to participate, 3042 consented to participate and completed the baseline assessment (75% participation rate); 1514 were men (18-87 years, mean age: 46±14 years) and 1528 were women (18-89 years, mean age: 45±14 years). All participant interviews were carried out by trained personnel (i.e., cardiologists, general practitioners, dietitians and nurses), who administered standard questionnaires. Details regarding the aims and methods of the ATTICA study have been previously reported (10).

Baseline assessments

The baseline evaluation included socio-demographic, biological, clinical and lifestyle characteristics. Participants with blood pressure levels greater or equal to 140/90 mmHg -or prescribed medication- were classified as hypertensive. Hypercholesterolemia was defined as having total cholesterol >200mg/dl or being prescribed lipids-lowering agents. Diabetes mellitus was defined according to the American Diabetes Association criteria (i.e., a blood glucose levels >125 mg/dl or being treated for diabetes). Smokers were defined as individuals who smoked at least one cigarette per day or had ceased smoking within the previous year; all others were defined as non-smokers. Consumption of various foods and beverages were measured as an average intake per week during the past year using a validated semi-quantitative food–frequency questionnaire, from the Unit of Nutritional Epidemiology of Athens Medical School (11). Based on the Mediterranean diet pyramid, the MedDietScore, which ranged from 0 to 55 (12) for each participant was calculated electronically, with higher scores indicating a greater level of adherence to Mediterranean Diet. Body Mass Index (BMI) was calculated as weight (in kilograms) divided by standing height (in meters squared). Waist (in cm) and hip (in cm) circumferences were also measured and waist-to-hip ratio was calculated.

Physical activity evaluation

A translated version of the validated "International Physical Activity Questionnaire" (IPAQ) was administered. This tool is suitable for assessing population levels of self-reported physical activity (13). The short version of IPAQ (7 items) provided information on weekly time engaged in walking, vigorous-intensity and moderate-intensity activity as well as time being sedentary. Participants were instructed to record all physical activity episodes with duration of at least 10 minutes, since this is considered to be the minimum time required to achieve a health benefit. In terms of the intensity of physical activity, the categorical analysis grouped the subjects in the following three categories of physical activity level which were developed based on the IPAQ guidelines for physical activity (14). Therefore, participants were classified as inactive/insufficiently active, sufficiently active and highly active (health enhancing physical activity; a high active category). This was based on the following criteria: sufficiently active (SA), when any of the following three criteria were met: a) 3 or more days of vigorous activity of at least 20 minutes per day, b) 5 or more days of moderate-intensity activity or walking of at least 30 minutes per day, or c) 5 or more days of any combination of walking, moderate-intensity or vigorous-intensity activities achieving of at least 600 MET-min/week; highly active or health enhancing physical activity (HEPA) which was defined when any of the following criteria were met: a) vigorous-intensity activity on at least 3 days achieving a minimum of at least 1500 MET-minutes/week, or b) 7 days of any combination of walking, moderate-intensity or vigorous intensity activity achieving a minimum of at least 3000 MET-minutes/week. Finally, the third category was inactive/insufficiently active (INA), which is the lowest physical activity level category and was classified when no criteria were met to classify the individual in either of the other two categories.

Follow-up evaluation (2011-2012)

During 2011-2012, the 10-year follow-up was performed. Of the n=3042 participants, n=2583 were traced during the follow-up period (85% retention rate). Participants were initially contacted by telephone calls, and then the trained study personnel conducted face-to-face interviews. Study investigators performed a detailed evaluation of the participants' medical status using standardized procedures (15). For the present work, data from n=2020 participants with accurate CVD evaluation were included in the analysis.

Ethics

The Institutional Ethics Committees of the First Cardiology Clinic, School of Medicine, University of Athens and Harokopio University, granted ethical approval.

Statistical analysis

Unadjusted, nonfatal, and fatal incidence rates of combined CVD outcomes (i.e., CHD or stroke) were calculated as the ratio of new cases to the number of people participated in the follow-up. For the description of participant's characteristics, continuous variables are presented as mean values and standard deviation, while categorical variables are presented as relative frequencies. Comparisons between mean values of normally distributed variables between those who developed an event and the rest of the participants were performed using Student's t-test, after controlling for equality of variances using the criterion suggested by Levene and for continuous variables that were not normally distributed (i.e., C-reactive protein levels), Mann–Whitney nonparametric test was applied. In the case of categorical variables, the tested hypotheses were performed with chi-square test. Comparisons between differences of mean values of normally distributed variables among groups of physical activity were tested using the analysis of variance (ANOVA) after controlling for homoscedacity. Kruskal–Wallis test were applied to evaluate the differences in the distributions of the skewed variables among the categories of physical activity. In order to evaluate differences between specific category levels of physical activity (i.e., inactive/ insufficiently active, sufficiently active and highly active), post-hoc analysis using the Bonferroni correction rule to adjust for the inflation of type I error were applied. The assumption of normality was tested using Q-Q and P-P plots. Nested binary logistic regressions were applied with CVD as the dependent variable to assess the effect of PA level category. Since a significant interaction between gender and physical activity levels were observed, further stratified analysis by gender were performed. The Hosmer and Lemeshow's goodness of-fit test were calculated in order to evaluate the model's goodness-of-fit. All reported *P*-values are based on two-sided hypotheses and compared to a significance level of 5%. For all the statistical calculations the SPSS version 21 was used (IBM, SPSS).

RESULTS

During the study period (2002-2012), the 10-year fatal and nonfatal CVD incidence were n=317 cases (15.7%); of them, n=198 were men (19.7% of the male participants developed CVD) and n=119 were women (11.7% of the female participants developed CVD), (p for gender<0.001). With respect to physical activity categories, 60.9% of men and 66.9% of women were classified, as being inactive/insufficiently active and only 8.8% of men and 6.9% of women were highly active. Moreover, 18.4% of inactive/ insufficiently active participants, 11.6% of sufficiently active individuals and 7.5% of highly active participants developed a CVD event (p<0.001). Concerning fatal CVD events, 71.7% were developed among inactive/ insufficiently active individuals and only the 13.0% of them was among the HEPA individuals, whilst for non-fatal CVD events, 63.1% of these occurred in inactive/insufficiently active individuals, with only 8.9% of these events occurring among HEPA participants.

Table 1 provides a description of the study participants by gender and CVD status at 10-year. Participants from both genders who developed CVD tended to be older, had increased systolic/diastolic blood pressure, blood lipids (total cholesterol, LDL-cholesterol, triglycerides), glucose, C-reactive protein and anthropometric indices (BMI, waist circumference, waist to hip ratio) as well as smoking more cigarettes per year, when compared with CVD free subjects. Furthermore, individuals with CVD incidence had lower level of adherence to Mediterranean diet, but reported a higher educational status when compared to those without CVD (all p<0.001). Men who did not develop CVD within the follow-up period spent less time being sedentary compared to CVD-free women (p<0.001). Moreover, CVD-free women spent more time sitting as compared to women who developed CVD (p<0.001).

[Table 1]

The characteristics of the men and women participated in this study, by physical activity category are provided in ***Table 2***. Inactive/insufficiently active (sedentary) men and women had higher BMI (p=0.001), waist circumference (p<0.001), waist to hip ratio (p=0.01) and C-reactive protein (p<0.05) compared to the highly active individuals, of the same gender. Additionally, inactive/insufficiently active men were more likely to be current smokers and hypertensive in comparison to highly active men (all p<0.05). Additionally, inactive/ insufficiently active women were likely to be older and completed fewer years of school than highly active women (all p<0.05).

[Table 2]

Nested logistic regression analyses were conducted to assess the potential effects of physical activity category on CVD (e.g., incidence vs. absence) taking into consideration demographic, lifestyle and clinical risk factors (age, sex, years of school, diabetes, hypertension, hypercholesterolemia, C-reactive protein, sedentary time, *MedDietScore*, sedentary time, smoking, BMI and waist to hip ratio) within the whole cohort sample. The crude, unadjusted, analysis revealed that sufficiently active and highly active individuals had decreased risk of CVD by 58% (95% Confidence Interval (CI): 0.30, 0.58) and 70% (95%CI: 0.15, 0.56), when compared to inactive/insufficiently active individuals, respectively. The interaction between gender and physical activity was tested using the same model. The interaction term (gender and PA category), in the crude analysis adjusted for age, was found to be significant (p=0.005) and the analysis was further stratified by gender. No significant interaction was detected between age and PA category (p=0.743) (*data not shown*). As expected, PA category was an independent predictor of CVD risk for men, but not for women. More specifically (Model 1) ***(Table 3)***, only those who were sufficiently active were protected against CVD when compared to inactive/ insufficiently active individuals (OR=0.45, 95%CI: 0.27, 0.73). When diabetes, hypertension, hypercholesterolemia, and C-reactive protein were added to the model in the analysis (Model 2), results related to the effect of physical activity category as well as of age did not change, while C-reactive protein increased the risk of CVD in men by 85% (95%CI: 1.02, 3.36 and 9.1% (per one-year increase) (95%CI: 1.01, 1.18), respectively. Finally, when years of school, smoking, *MedDietScore*, sedentary time and waist to hip ratio were included in the analysis (Model 3), sufficient physical activity in comparison to inactivity remained a protective factor for men (OR=0.48, 95%CI: 0.24, 0.97), but physical activity had no longer any influence on CVD risk in women ***(Table 3).*** [Table 3]

DISCUSSION

The current study comprehensively evaluated the effect of physical activity categories on CVD incidence, in a prospective representative cohort of the Greek adult population. The results support the notion that physical activity is associated with decrease in risk of 10-year CVD incidence; however, this finding was confirmed only for sufficiently active men after the moderating effect of gender was taken into account, along with adjustment for clinical and lifestyle risk factors. Considering these findings from a public health perspective, these findings potentially support the targeting of the adult male population, especially to encourage the adoption of regular moderate physical activity, which could result in an independent decrease of 10-year CVD risk. It should be mentioned that the number of females that were highly active was relatively small; thus, this null finding could potentially be differentiated in a larger sample.

Several biological mechanisms have been proposed as mechanisms to explain for protective effects of physical activity with respect to CVD risk and incidence. Specifically, physical activity/exercise is thought to favorably influence the atherosclerotic process, endothelial function, plasma lipid/lipoprotein profile, blood pressure levels, availability of oxygenated blood for heart muscle needs, and heart rhythm disturbances, while also enhancing cardiac mechanical and metabolic function (16-18), as well as a metabolically healthier distribution of body fat, reduced incidence of obesity and risk of developing type 2 diabetes mellitus (19). In the current study, when these biological and clinical risk factors were taken into account, the risk estimates for women became non-significant, whilst for men, only the sufficiently active category was found beneficial as compared to the inactive/insufficiently active category. It might be suggested that other mechanisms could lead to a decrease in CVD risk which could explain the observed inverse association, including improvement in HDL-cholesterol level, thrombotic function, platelet function, fibrinogen, and fibrinolysis (20).

An interesting finding of this study is that despite the prevalence of CVD incidence being considered the leading cause of death, almost two in three of participants were considered to be physically inactive/ insufficiently active according to international criteria (14). The seriousness of the problem of inactivity was further confirmed by results in the present study indicating a strong relation between PA category and CVD risk. A sufficient level of physical activity was significantly and inversely associated with the incidence of CVD independent of age, years of school, smoking, MedDietScore, anthropometric indices (waist to hip ratio) and biological risk factors (e.g. diabetes mellitus, hypercholesterolemia, hypertension and C-reactive protein), in males. However, this association was not replicated in women, suggesting that a moderating effect of gender on the effect of physical activity with respect to CVD risk (9). The latter could be attributed to several gender differences, including the decline of ventricular myocytes, which are seen to decrease in men but not in women (9) along with differences in mechanical and physiological responses to exercise (21).

The finding that a physically active lifestyle is associated with a lower CVD incidence has been suggested by a number of studies. Specifically, findings from 52 countries (INTERHEART study), suggested that approximately 80% of CVD-related morbidity and mortality could be preventable by moving to a healthier lifestyle (physical activity, healthy diet, healthy body weight and not smoking) (22). The review of Blair et al. in 2001, including 67 prospective observational studies, concluded that regularly physically active individuals had reduced risk for CVD compared to sedentary individuals and there were consistent evidence for an inverse dose-response effect across physical activity categories (23). Additionally, a review of Kruk in 2007, suggested that physical activity is associated with a risk reduction of 49% for CVD (24), and a meta-analysis of 21 prospective studies found that a higher level of leisure time PA and moderate level of occupational PA reduced the overall risk of CVD among men and women by 20-30% and 10-20%, respectively (25). Likewise, in a dose response meta-analysis in women, physical activity was associated with reduced risk (20-30%) of overall-CVD among women in a dose-response trend (26). The potential of physical activity to moderate CVD risk needs to be considered together with an individual's perceptions of opportunities for physical activities, as these have been recently associated with the ability to engage in exercise (27). This is a key finding that should alert public health policy makers and politicians to support access and the availability of sports and recreational facilities for all.

Limitations

Several limitations should be considered in light of our findings. Baseline evaluations were performed only on one occasion, and may be predisposed to measurement error, but these are the standard procedures typically followed in large observational studies, and as such, these results are comparable to the other studies. Additionally, the level of physical activity was self-reported rather than measured with an objective tool (such as a pedometer or accelerometer, which have been proposed by other research groups (28, 29)) and as such could also be prone to measurement bias as well as to over and under-reporting issues. However, the use of IPAQ to estimate physical activity status is widely accepted as valid and has been widely used in other similar large observational studies, so data can be seen as being comparable to that published by other groups. Another important limitation that has to be considered is that the IPAQ questionnaire was used to assess the physical activity level for all age-groups, whilst recently (30), there have been doubts raised regarding its performance in an elderly population. Unfortunately, this was not known during the baseline assessments in the ATTICA study, and thus, the IPAQ was administered for all individuals within the study. However, this concern potential only applies to a small proportion of the overall study sample (7.9%). Strengths of the present study include its prospective design and long duration, having a large, representative sample that underwent detailed assessments biological and lifestyle risk factors, which provided the ability to adjust for potential confounders.

Conclusions

This study provides further evidence concerning the beneficial effect of moderate physical activity levels on 10-year incidence of CVD, reinforcing the importance of maintaining a physically active lifestyle. This association persisted following the adjustment of potential confounders in males, but not for females, which could be attributed to different biological mechanisms, which link PA with CVD risk. However, more research is necessary to elucidate these mechanisms and explain these findings.

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Table 1. Demographic, anthropometric and lifestyle characteristics based on the 10-year incidence of CVD, in Greek men and women of the ATTICA study (n=2020), at baseline (2001-2).

	CVD event free		CVD events	
	Men (n=807)	**Women (n=896)**	**Men (n=198)**	**Women (n=119)**
Age (years)	42.7 (13.6) *	43.5 (12.4) *	55.7 (12.8)	58.3 (13.1)
Current smoking (%)	64.0*	45.0*	71.0	34.0
Packs of cigarettes per year	520 (486)*	338 (325)	867 (719)	395 (312)
Hypertensive (%)	36.0 (0.5)*	21.0 (0.4) *	53 (0.5)	45 (0.5)
Systolic blood pressure (mmHg)	125 (16.3) *	117 (17.9) *	134 (18)	131 (21.3)
Diastolic blood pressure (mmHg)	81.3 (11.3) *	75.7 (10.9) *	83.3 (11.6)	81.2 (11.8)
Hypercholesterolemia (%)	43.9*	35.9*	58.4	57.9
Total cholesterol (mg/dl)	195 (41) *	190 (41) *	207 (46)	210 (45)
LDL-cholesterol (mg/dl)	125 (37.3) *	118 (36.5) *	134 (44.4)	131 (37.7)
Triglycerides (mg/dl)	134 (86)*	94.5 (54.1) *	183 (165)	126 (66.8)
MedDietScore (0-55)	24.4 (5.2) *	28.1 (6.6) *	22.7 (6.3)	23.8 (7.0)
Body mass index (kg/m^2)	27.3 (3.9)*	25.0 (4.7) *	28.5 (4.1)	27.1 (5.1)
Waist (cm)	96.9 (12.9) *	82.5 (13.5) *	103 (11.5)	89.0 (13.8)
Waist-to-hip ratio	0.92 (0.09) *	0.79 (0.08) *	0.97 (0.09)	0.84 (0.08)
Diabetes (%)	6.0 *	4.0 *	22.0	18.0
Blood glucose (mg/dL)	93.5 (22.2) *	89.7 (21.3) *	106 (34.8)	97.7 (27.4)
C-reactive protein (mg/L)	1.1 (0.51,2.1) *	0.94 (0.39,2.24) *	1.5 (0.69,2.8)	1.5 (0.59,3.7)
Years of school (n)	12.6 (3.5) *	12.4 (3.7) *	11.1 (4.2)	9.5 (4.1)
Sedentary time (hours/day)	6.80 (2.29)	7.39 (2.58)*	6.81 (2.35)	6.89 (2.52)

Descriptive statistics are mean (SD) for normally distributed variables or median (1st quartile, 3rd quartile) for skewed variables and relative frequencies for categorical variables. P-values derived from Student's t-test for the normally distributed variables and the Mann–Whitney test for the non-normally distributed variables (C-reactive protein) or the chi-square test for the categorical variables. *p<0.05, for the comparisons between those with CVD event and CVD event free, by sex.

Table 2. Demographic, anthropometric and lifestyle characteristics based on the 10-year incidence of CVD by physical activity category, in Greek men and women of the ATTICA study at baseline (2001-2).

Men	**INA *(n=613)***	**SA *(n=304)***	**HEPA *(n=89)***	***p*** ┼
Age (years)	45.5 (12.4)	46.9 (14.7)	44.8 (15.3)	0.238
Years of school (n)	12.3 (3.7)	12.3 (3.7)	12.6 (3.4)	0.778
Current smoking (%)	70.1*	60.5**	53.9	0.001
Hypertensive (%)	39.2*	41.7	28.6	0.093
Diabetes (%)	9.6	7.2	7.1	0.462
Hypercholesterolemia (%)	47.7	46.1	42.7	0.647
MedDietScore (0-55)	24.1 (5.5)	24.2 (5.4)	23.6 (5.4)	0.481
Body mass index (kg/m^2)	27.8 (4.0)* a	27.0 (3.8)	26.4 (3.1)	0.001
Waist (cm)	99.1 (13.4) * a	96.7 (11.6)	92.3 (9.7)	<0.001
Waist-to-hip ratio	0.94 (0.10) *	0.92 (0.07)	0.91 (0.08)	0.01
C-reactive protein (mg/L)	1.3 (0.62,2.6)*	0.92 (0.44,2.1)	0.74 (0.44,1.5)	0.026
Sedentary time (hours/day)	8.19 (1.64)*	4.79 (1.51)	4.63 (0.81)	<0.001
Women	**INA *(n=679)***	**SA *(n=266)***	**HEPA *(n=70)***	***p*** ┼
Age (years)	45.1 (13.8) *	44.2 (15.8)	40.9 (14.0)	0.053
Years of school (n)	11.8 (3.9) *	12.4 (3.7)	13.1 (3.9)	0.003
Current smoking (%)	46.4	37.2**	48.5	0.028
Hypertensive (%)	25.5	21.8	19.3	0.339
Diabetes (%)	6.3	5.2	1.4	0.248
Hypercholesterolemia (%)	40.4	36.1	30.1	0.152
MedDietScore (0-55)	27.5 (7.0)	27.8 (6.8)	26.9 (4.7)	0.596
Body mass index (kg/m^2)	25.6 (4.9)*	24.9 (4.8) **	22.9 (3.2)	<0.001
Waist (cm)	84.1 (13.4) *	82.4 (14.5) **	77.8 10.9)	0.001
Waist-to-hip ratio	0.80 (0.08)*	0.80 (0.08)	0.77 (0.08)	0.027
C-reactive protein (mg/L)	1.02 (0.42,2.5) *	0.86 (0.4,2.4)	0.66 (0.32,1.54)	0.048
Sedentary time (hours/day)	8.64 (1.93)*	4.57 (1.53)	4.56 (0.76)	<0.001

INA: inactive/insufficiently active, SA: sufficiently active, HEPA: health enhancing physically active. Descriptive statistics are presented as mean (SD) for normally distributed variables or median (1st quartile, 3rd quartile) for skewed variables and relative frequencies for categorical variables. ┼ P-values derived from analysis of variance for the normally distributed variables and the Kruskal–Wallis test for the non-normally distributed variables (C-reactive protein) or the chi-square test for the categorical variables. *p<0.05, for the comparisons between INA, and HEPA; **p<0.05, for the comparisons between SA and HEPA; [a] p<0.05 for the comparisons between INA and SA.

Table 3. Results (OR, 95%CI) from logistic regression models that used to evaluate the mediation effect of physical activity category on risk of CVD in Greek adults, by sex (2002-2012).

Predictors	Model 1 Initial model OR (95% CI)	Model 2 Full model OR (95% CI)	Model 3 Full model, plus confounders (OR 95% CI)
Men			
Age (per 1 year)	1.09 (1.07-1.11)	1.09 (1.07-1.11)	1.08 (1.06-1.10)
Physical activity category			
SA vs. INA	0.45 (0.27-0.73)	0.46 (0.28-0.76)	0.48 (0.24-0.97)
HEPA vs. INA	0.88 (0.47-1.66)	0.94 (0.49-1.80)	1.02 (0.45-2.28)
Hypertension (yes vs. no)		1.25 (0.83-1.87)	1.27 (0.84-1.92)
Hypercholesterolemia (yes vs. no)		1.27 (0.85-1.90)	1.19 (0.78-1.79)
Diabetes (yes vs. no)		1.85 (1.02-3.36)	1.74 (0.95-3.17)
C-reactive protein (per 1 mg/L)		1.09 (1.01-1.18)	1.08 (0.99-1.17)
Years of school (per 1 year)			0.97 (0.92-1.02)
MedDietScore (0-55) (per 1 unit)			0.98 (0.95-1.02)
Current smoking (yes vs. no)			1.66 (1.04-2.66)
Sedentary time (per 1 hour/day)			1.00 (0.88-1.15)
Waist to hip ratio (per 1 cm)			1.67 (0.20-14.15)
Women			
Age (per 1 year)	1.10 (1.08-1.12)	1.09 (1.07-1.11)	1.07 (1.05-1.10)
Physical activity category			
SA vs. INA	1.44 (0.84-2.48)	1.48 (0.86-2.56)	1.45 (0.67-3.13)
HEPA vs. INA	0.82 (0.30-2.27)	0.89 (0.32-2.48)	0.87 (0.27-2.77)
Hypertension (yes vs. no)		1.44 (0.85-2.43)	1.45 (0.84-2.50)
Hypercholesterolemia (yes vs. no)		0.96 (0.58-1.58)	0.89 (0.53-1.48)
Diabetes (yes vs. no)		1.39 (0.62-3.10)	1.29 (0.57-2.93)
C-reactive protein (mg/L)		1.06 (0.98-1.15)	1.05 (0.97-1.14)
Years of school (per 1 year)			0.93 (0.87-1.00)
MedDietScore (0-55) (per 1 unit)			0.97 (0.92-1.01)
Current smoking (yes vs. no)			1.29 (0.76-2.19)
Sedentary time (per 1 hour/day)			0.97 (0.84-1.11)
Waist to hip ratio (per 1 cm)			1.10 (0.05-22.6)

INA: inactive/insufficiently active, SA: sufficiently active, HEPA: health enhancing physically active.
Model 1: Age and Physical activity category
Model 2: Model 1 + Hypertension, Hypercholesterolemia, Diabetes, C-reactive protein, School years
Model 3: Model 2 + MedDietScore, Smoking, Sedentary time and Waist to hip ratio.

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