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Longitudinal trends in physical activity levels and lifetime cardiovascular disease risk: insights from the ATTICA cohort study (2002-2022)

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Keywords

Physical activity trajectories • Lifetime CVD risk • ATTICA study • Socio-economic determinants

Summary

Objective. *To evaluate trends in physical activity levels and their associations with demographic characteristics, health status, and lifetime cardiovascular disease (CVD) risk.*

Methods. *A longitudinal analysis was conducted using data from 987 males and 1,001 females (45 ± 12 years old) participating in the ATTICA cohort study. Physical activity levels were assessed at baseline (2001-2002) and subsequent follow-ups (2006, 2012, and 2022). Four physical activity trajectories according to participants' physical activity tracking were defined, i.e., consistently active/inactive and changed from active/inactive. Twenty-year incidence of hypertension, hypercholesterolemia, and diabetes were evaluated in relation to physical activity trajectories; the life-table method was utilized to forecast the lifetime CVD risk (death without CVD was regarded as a competing event).*

Results. *in total, 47% of the participants were categorized as being consistently inactive, whereas only 9% of males and 15% of females sustained physical activity levels throughout the 20-year follow-up period (p < 0.001). Participants being consistently inactive were from lower socioeconomic backgrounds (p = 0.002). Transitioning to being physically active was associated with higher education level and being married (p < 0.001). Consistently active individuals had up to 35% reduced lifetime CVD risk, and lower 20-year incidence of hypertension, and hypercholesterolemia (p < 0.01); no association was observed regarding diabetes incidence.*

Conclusions. *Promoting and maintaining regular physical activity throughout lifespan is crucial for reducing lifetime CVD risk and related risk factors. Tailored interventions addressing demographic and socioeconomic factors may help enhance cardiovascular health outcomes.*

Introduction

Accumulating level of evidence during the past decades strongly suggest that even moderate physical activity levels are significant contributors for wellness, and longevity. The World Health Organization (WHO) has developed the "2018-2030 Action Plan for More Active People For A Healthier World", according to which physical activity is being recognized as a crucial lifestyle parameter across all ages, that can and should be integrated into people's everyday lives [1, 2]. This plan is also supported by several Organizations and medical societies suggesting that people of all ages should be engaged in regular physical activities to reduce morbidities and all-cause mortality [3-5].

Despite the plethora of health benefits presented in the scientific literature and supported by public health campaigns, a gradual shift towards a more sedentary lifestyle has been systematically observed over the past few years [6-8]. A combination of environmental, social, psychological, and physical factors can contribute to the adoption of a sedentary lifestyle. The current technological advancements and societal norms seem fostering a culture of prolonged sitting and reduced engagement in physical activities. For example, because of urbanization, limited access to safe outdoor spaces, sports facilities, or recreational areas is evident in many cities around the world, a fact that discourage engagement in physical activities [6]. Busy daily schedules and demanding workflow also make challenging for many people to prioritize physical activity in their daily life. Moreover, in some cultures, there may be less emphasis placed on physical activity, leading to a more sedentary lifestyle [7, 8].

However, the majority of evidence comes from ecological studies, and few observational studies have ventured into the assessment of long-term physical activity trajectories and their intersection with people's characteristics, leaving a void in our understanding of the dynamic interplay between lifestyle behaviors and

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health over time. Therefore, it could be, at least partially explained, why prevention strategies, programs and population-based interventions have not been as efficient as expected so far.

Considering the gap in our understanding of the determinants of maintaining a physically active level throughout lifespan and its effect on health, the aim of the present study was to investigate the association of physical activity levels over a 20-year period of apparently healthy adults with various socio-demographic and clinical characteristics, as well as with cardiometabolic outcomes (*i.e.*, hypertension, hypercholesterolemia, and type II diabetes mellitus) and lifetime CVD risk. We hypothesize that individuals with consistently active lifestyles will exhibit lower incidence rates of hypertension, hypercholesterolemia, and diabetes mellitus, leading to a reduced lifetime risk of CVD compared to those with consistently sedentary behaviors.

Material and methods

Study design

The ATTICA study is a prospective epidemiological cohort study that aims to record the distribution and patterns of several socio-demographic, lifestyle, clinical, biochemical, and psychological factors related to CVD, and to investigate the relationships between these factors and long-term incidence of CVD.

Setting and participants

The study was carried out in the Attica region in Greece, with 78% coming from urban municipalities, including the capital city, Athens. The baseline participant sample consisted of 3,042 individuals (out of 4,056 who were initially invited, 75% participation rate), all free of CVD, cancer, and other chronic inflammatory diseases, as established by the physicians of the study during the baseline examination. The sampling procedure was random and stratified based on sex, age group, and region, in accordance with the 2001 census.

Detailed information about the objectives, design, sampling procedure, and methodology of the study can be found in previously published papers [9-11].

Bioethics

The ATTICA study adheres to the ethical guidelines of the Declaration of Helsinki and has been approved by the Ethics Committee of the First Cardiology Department of the National and Kapodistrian University of Athens (#017/01.05.2001), and the Ethics Committee of the Harokopio University (#38/29.03.2022). All participants were informed about the objectives and procedures of the study, and they provided their written consent to participate.

Follow-up examinations

The study performed 3 follow-up examinations, at 5-years (in 2006), 10-years (in 2012) and 20-years (in 2022), following the baseline assessment (in 2001-2002). Development of CVD or any other disease (including fatal events), as well as detailed clinical status, lifestyle characteristics (*i.e.*, dietary habits, physical activity level and smoking status), and psychological status, were repeatedly assessed in all follow-up periods following the same methodology [10, 11]. Specifically, in 2012, 2,583 participants were allocated and agreed to re-examined at the 10-year follow-up (85% participation rate), and in 2022, 2,169 participants were found and agreed to participate at the 20-year follow-up (participation rate of 71%). Among those who were lost to follow-up (n = 873 individuals), 771 could not be reached due to changes in their contact information or errors in their addresses or phone numbers, while 102 declined to participate in the screening. For deceased participants, information was gathered from relatives and death certificates.

When comparing the age and sex distribution of this sub-sample with the baseline group, no significant differences were found (p-values > 0.80).

Measurements

Physical activity status evaluation

The translated version of the validated into Greek population by Papathanasiou et al., International Physical Activity Questionnaire (IPAQ) of weekly energy expenditure was used [12]. The frequency (times per week), duration (in minutes) and intensity of leisure time physical activity (LTPA) during a usual week was recorded. Intensity was graded in qualitative terms, based on the metabolic equivalent of tasks (METmin/week), as: light (expended calories < 4 Kcal/min, *i.e.*, walking slowly, stationary cycling, light stretching *etc.*), moderate (expended calories 4-7 Kcal/min, *i.e.*, briskly walking, outdoor cycling, swimming with moderate effort *etc.*) and high (expended calories > 7 Kcal/min, *i.e.*, briskly walking uphill, long-distance running, cycling fast or racing, swimming fast crawl *etc.*).

For the present analysis, participants were classified as inactive (sedentary or light physical activity), and active (moderate or high physical activity) according to the METmin/week [13].

Four trajectories of physical activity were formed regarding the longitudinal tracking, 2002-2012, in the physical activity levels of the participants, *i.e.*, consistently inactive, became inactive from physically active, became active from physically inactive, consistently active.

Socio-demographic and behavioural characteristics

Demographic characteristics included, age (in years), sex (male, female), family status (single, married or cohabitated, divorced, widowed), financial status (average annual income during the past three years), occupational status (employed, unemployed, retired, housekeeping) and education level. Specifically, the educational level of the participants (as a proxy of social status) was measured in years attending formal school, college and/or university.

A validated and reliable semi-quantitative food frequency questionnaire was utilized for dietary assessment, with habitual food intake expressed as servings per day or week [14]. Adherence to a Mediterranean-type diet was evaluated using the MedDietScore, an a-priori diet index comprising of 11 food group items traditionally consumed the region and has been found valid and reliable in measuring adherence to the Mediterranean dietary pattern [15]. The MedDietScore ranges from 0 to 55 points. Higher values of the MedDietScore signify enhanced adherence to the traditional Mediterranean diet. The median value of the MedDietScore was used to classify participants into a high (*i.e.*, MedDietScore > 27) and a low (*i.e.*, MedDietScore ≤ 27) adherence to the Mediterranean-type diet [15].

Clinical assessment

At baseline and at each follow-up examination, blood samples were collected after 12 hours of fasting and avoiding of alcohol. The biochemical evaluation was carried out in the same laboratory that followed the criteria of the World Health Organization Lipid Reference Laboratories. According to the European Atherosclerosis Society and the European Society of Cardiology guidelines, participants with total serum cholesterol levels greater than 200 mg/dL or those taking lipid-lowering agents were classified as having hypercholesterolemia; participants with blood sugar > 125 mg/dL or the use of antidiabetic medication were classified as having diabetes mellitus. Arterial blood pressure was obtained with subjects in sitting position and calmed for 30 minutes. Participants whose average systolic/diastolic blood pressure levels were greater or equal to 140/90 mmHg or taking antihypertensive medication were classified as having hypertension. Body mass index (BMI) was calculated as weight (in kg) divided by standing height (in m squared). Obesity was defined as BMI > 29.9 kg/m^2. Details about the methods and definitions used may be found in previous publication of the study [9].

Follow-up assessment

Development of hypertension, hypercholesterolemia, diabetes melitus (type 2), as well as fatal or non-fatal CVD events (*i.e.*, coronary heart disease, stroke, or any other type of CVD) was assessed at all follow-up examinations, based on International Classification of Diseases (ICD)-10 version [16]. For individuals who suffered multiple events (*e.g.* individuals who might had first suffered from stroke and then had coronary heart disease) the first outcome was considered as the endpoint, and the consequent event was recorder as well for further testing of potential competing risks.

Statistical analysis

Continuous variables were expressed as mean values accompanied by their standard deviations. Categorical variables were presented as relative frequencies (percentages). The associations among categorical variables were assessed using Pearson's chi-squared test. Comparisons of mean values for continuous variables were conducted employing independent samples t-tests or Analysis of Variance (ANOVA), with Levene's test utilized to ensure equality of variances. In instances where variances were found to be unequal (Levene's test p-value < 0.05), the Welch's t-test was employed. Adjustment for multiple comparisons was performed using the Bonferroni correction method. The normality of continuous variables (*i.e.*, cholesterol and triglycerides levels) was assessed through P-P plots. Incidence rates were compared using 95% confidence intervals (CI) derived from the Normal approximation to the Poisson distribution, with p-values obtained from the 4-sample test for equality of proportions with continuity correction. The lifetime risk estimates for CVD were computed using age and sex-adjusted life-table techniques, considering the competing risk of mortality and projecting outcomes until the age of 85 years for the last participant in the cohort. Modified life-table techniques were utilized to account for the competing risk of mortality. To compare age and sex-adjusted lifetime risks across different physical activity trajectories, a two-tailed Z-test was employed. All reported p-values were based on two-sided hypotheses. Statistical analyses were conducted using STATA version 17 (STATA Corp, College Station, Texas, USA).

Results

Participants characteristics according to trajectories of physical activity levels

Thirty nine percent (39%) of males and 33% of females were classified as physically active at baseline examination (in 2002), 31% males and 26% females at 5-year follow-up (in 2005), 26% males and 19% females at 10-year follow-up (in 2012), and 30% males and 32% females at 20-year follow-up (in 2022). A progressive decrease in physical activity levels was observed ($p < 0.001$). In Figure 1 the distribution of physical activity levels at each time-point of the follow-up is illustrated, by sex and age group of the participants, while in Figure 2, the physical activity trajectories of participants are displayed, categorized by age, sex, and socioeconomic status. Specifically, this heatmap illustrates the predominant trajectory within each subgroup, determined by the highest probability of participant association. During the 20-year observation period, in total, 47% of the participants were classified as always inactive, 23% as became inactive from physically active, 18% as became active and, only 9% of males and 15% of females sustained physical activity levels ($p < 0.001$) (Tab. I). Moreover, participants who stopped being physically active during the follow-up period were older than those who were consistently active (43 ± 12 years *vs* 40 ± 12 years, $p = 0.002$), and participants who started physical activity were the

Fig. 1. Distribution of physical activity status at each time-point, by sex and age group of the participants; ATTICA study (2002-2022).

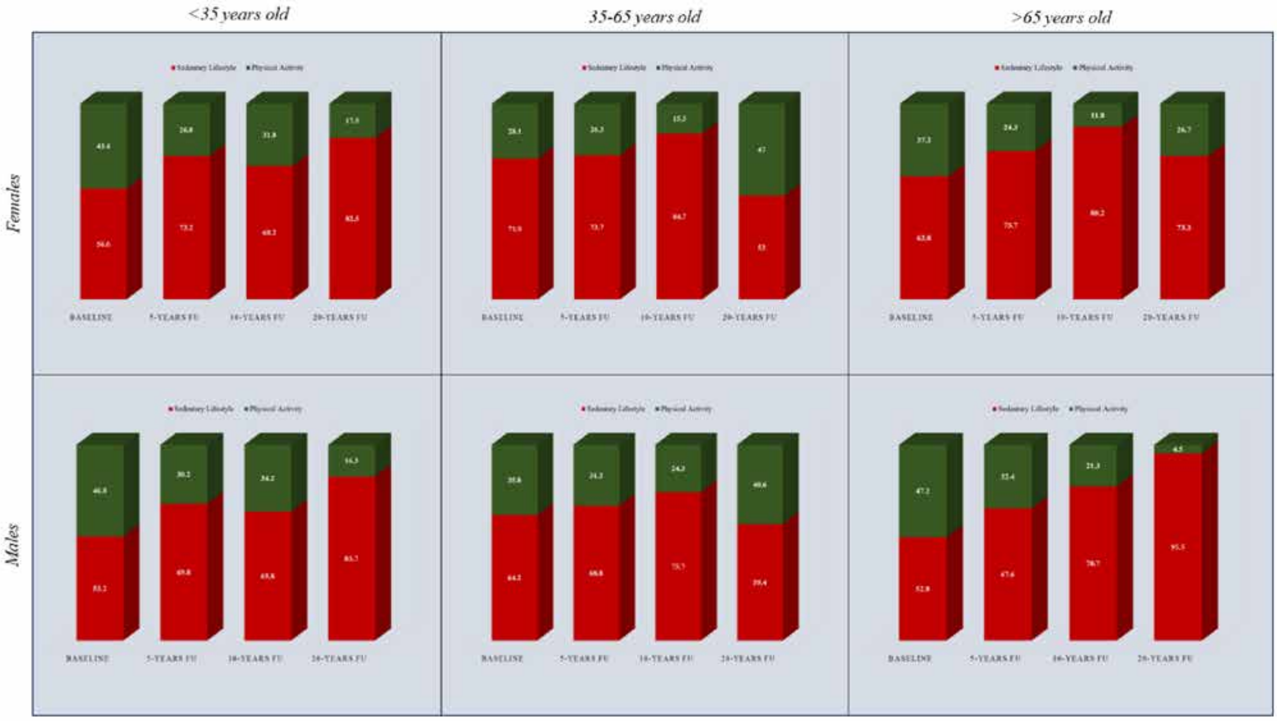
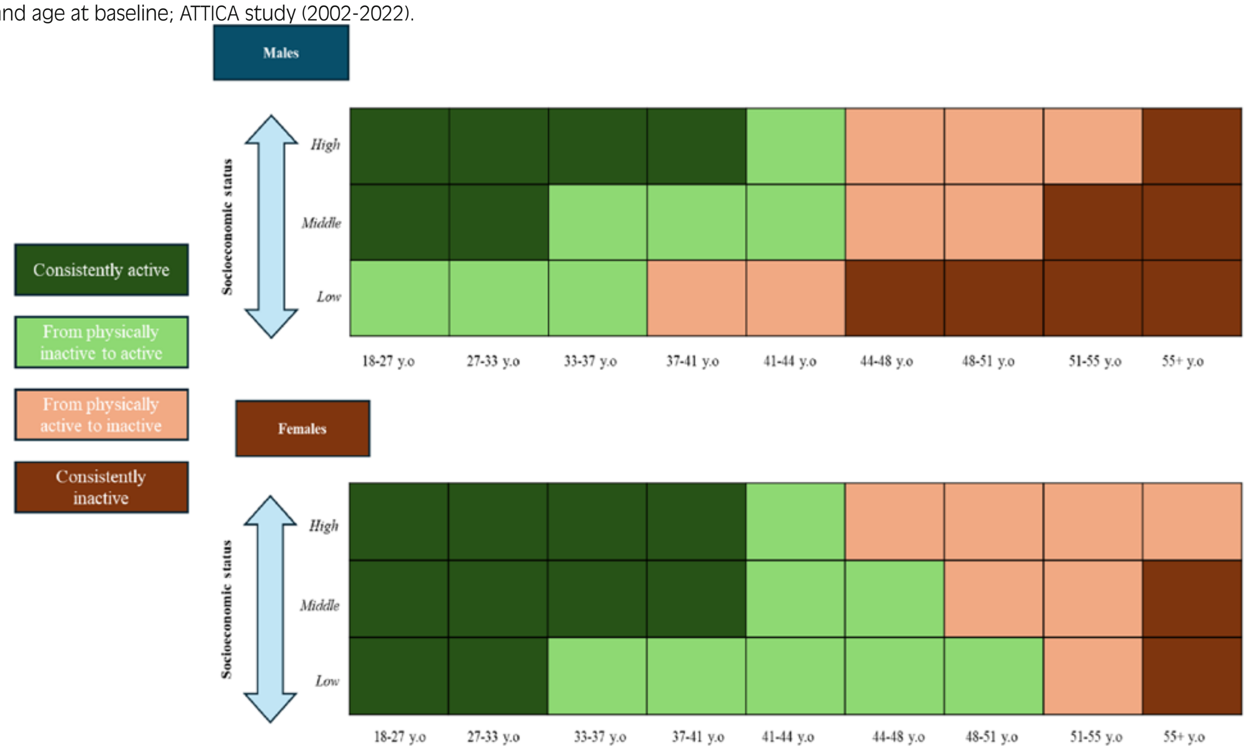


Fig. 2. Heatmap presenting the time trajectories of physical activity status in males and females, stratified by their socioeconomic status and age at baseline; ATTICA study (2002-2022).



youngest among all other trajectories (35 ± 13 years, $p < 0.01$).

The social and demographic characteristics of participants categorized by their physical activity trajectory during the follow-up period are presented in Table I. Participants identified as consistently physically inactive where from lower socioeconomic background (especially males) and had, particularly, lower education status. On the contrary, participants who transitioned to being physically active exhibited higher education level ($p < 0.001$ for both sexes) and were more likely of being married ($p < 0.05$ for both sexes).

Tab. I. Baseline sociodemographic characteristics of the ATTICA study participants, stratified according to their 20-year physical activity trajectory and sex; ATTICA study (2002-2022).

	Consistently inactive	From physically active to inactive	From physically inactive to active	Consistently active	p-value
Females (n = 1001)	472 (47%)	204 (20%)	181 (18%)	144 (15%)	
Age [in years; Mean (SD)]	38.5 (15.3)	31.1 (13.1)	41.9 (10.7)	42.7 (12.7)	< 0.001
Marrital status, %					
Never married	39.7	66.7	8.9	25.0	< 0.001
Married	52.1	33.3	82.1	68.2	
Divorced	3.4	0.0	7.1	6.8	
Widowed	4.8	0.0	1.8	0.0	
Years of education [Mean (SD)]	12.3 (3.2)	13.5 (2.6)	13.9 (4.1)	12.6 (3.7)	0.011
Socioeconomic status, %					
Low	12.9	2.1	6.1	16.7	0.002
Middle	68.8	66.0	39.4	53.3	
High	18.3	31.9	54.5	30.0	
Males (n = 987)	466 (47%)	245 (25%)	190 (19%)	86 (9%)	
Age [in years; Mean (SD)]	41.5 (14.9)	39.3 (15.1)	42.6 (8.2)	44 (11)	0.308
Marrital status, %					
Never married	30.1	41.8	16.4	20.0	0.015
Married	68.5	54.4	82.0	77.1	
Divorced	0.0	3.8	1.6	2.9	
Widowed	1.4	0.0	0.0	0.0	
Years of education [Mean (SD)]	11.9 (3.9)	12.4 (3.8)	14.2 (2.1)	13.6 (2.8)	< 0.001
Socioeconomic status, %					
Low	15.4	7.7	0.0	4.0	0.012
Middle	53.8	55.8	42.9	52.0	
High	30.8	36.5	57.1	44.0	

p-value was based on the Pearson chi- square test (categorical characteristics) and on the One-way ANOVA (continuous characteristics). Participants' physical activity level was assessed through the short-form International Physical Activity Questionnaire. DS: standard deviation.

Tab. II. Baseline clinical characteristics of the ATTICA study participants, stratified according to their 20-year physical activity trajectory and sex; ATTICA study (2002-2022).

	Consistently inactive	From physically active to inactive	From physically inactive to active	Consistently active	p-value
Females (N = 1001)	472 (47%)	204 (20%)	181 (18%)	144 (15%)	
Total serum cholesterol [Mean (SD); mg/dl]	182 (42)	175 (42)	188 (44)	181 (38)	0.424
Triglycerides [Mean (SD); mg/dl]	96 (68)	79 (50)	87 (42)	86 (51)	0.305
HDL-cholesterol [Mean (SD); mg/dl]	52 (12)	56 (12)	55 (19)	52 (13)	0.275
LDL-cholesterol [Mean (SD); mg/dl]	109 (32)	104 (41)	119 (43)	111 (33)	0.189
Hypertension (% Yes)	22.7	8.3	19.2	14.3	0.095
Hypercholesterolaemia (% Yes)	37.5	22.2	28.1	29.5	0.328
Type II diabetes (% Yes)	7.1	1.5	6.8	2.3	0.125
Obesity (% yes)	17	13	6	1	0.032
Males (N = 987)	466 (47%)	245 (25%)	190 (19%)	86 (9%)	
Total serum cholesterol [Mean (SD); mg/dl]	193 (42)	187 (44)	204 (46)	203 (48)	0.097
Triglycerides [Mean (SD); mg/dl]	128 (82)	111 (58)	140 (87)	122 (66)	0.194
HDL-cholesterol [Mean (SD); mg/dl]	44 (11)	45 (11)	43 (10)	46 (10)	0.446
LDL-cholesterol [Mean (SD); mg/dl]	122 (38)	120 (38)	130 (36)	138 (49)	0.149
Hypertension (% Yes)	43.3	29.6	33.3	34.8	0.608
Hypercholesterolaemia (% Yes)	54.3	41.8	42.0	48.3	0.507
Type II diabetes (% Yes)	9.1	6.3	3.3	5.7	0.489
Obesity (% Yes)	21	22	12	13	0.278

p-value was based on the Pearson chi- square test (categorical characteristics) and on the One-way ANOVA (continuous characteristics) Participants' physical activity level was assessed through the short-form International Physical Activity Questionnaire. HDL: High Density Lipoprotein; LDL: Low Density Lipoprotein; SD: Standard Deviation.

As shown in Table II, no significant differences were observed among the four physical activity level trajectories and the baseline levels of various biochemical markers and clinical status of the participants. However, it is noteworthy that both males and females who remained physically inactive throughout the entire period had a higher prevalence

Tab. III. Incidence rate of hypertension, hypercholesterolaemia and type II diabetes mellitus (95% Confidence Interval) of the ATTICA study participants, stratified according to their physical activity trajectory; ATTICA study (2002-2022).

Incidence rate (95% CI)	Consistently inactive	From physically active to inactive	From physically inactive to active	Consistently active	p-value
Females					
Incidence rate of (per 1,000 Person-years):					
Hypertension	19.7 (9.7, 29.7)	19.3 (8.8, 29.7)	15.3 (9.7, 20.8)	5.7 (1.1, 10.3)	0.015
Hypercholesterolaemia	35.9 (21.3, 50.6)	35.6 (19.2, 52.1)	26.7 (16.0, 37.3)	24.0 (17.2, 30.9)	0.147
Type II diabetes	16.0 (10.6, 21.5)	14.4 (6.9, 22.0)	14.1 (5.4, 22.8)	10.1 (3.1, 17.1)	0.622
Males					
Incidence rate of (per 1,000 Person-years):					
Hypertension	35.1 (13.3, 56.8)	25.4 (17.2, 33.6)	16.7 (7.2, 26.1)	11.0 (4.2, 17.9)	0.009
Hypercholesterolaemia	54.3 (33.1, 75.7)	41.9 (30.6, 53.2)	29.1 (18.5, 43.7)	28.6 (8.8, 48.4)	0.037
Type II diabetes	26.8 (16.1, 37.5)	25.8 (16.1, 35.6)	20.9 (14.4, 27.4)	17.0 (5.9, 28.1)	0.449

95% Confidence Interval was based on the Normal approximation to the Poisson distribution, as described by Rosner, Fundamentals of Biostatistics (5th Ed); p-value was based on the 4-sample test for equality of proportions with continuity correction. IR: Incidence Rate; CI: Confidence Interval.

Tab. IV. Lifetime risk estimates (and 95%CI) for fatal and nonfatal CVD, at selected index age, in males and females, according to their 20-year physical activity trajectory; ATTICA study (2002-2022).

	Females			Males		
	40 yrs	50 yrs	60 yrs	40 yrs	50 yrs	60 yrs
Consistently inactive	51 (45, 57)	62 (59, 65)	73 (38, 81)	63 (44, 82)	76 (73, 78)	68 (62, 74)
From physically active to inactive	49 (41, 57)	59 (54, 64)	61 (23, 72)	60 (55, 64)	74 (69, 79)	62 (55, 68)
From physically inactive to active	48 (46, 51)	58 (54, 63)	60 (56, 63)	58 (45, 71)	72 (68, 76)	62 (52, 71)
Consistently active	45 (43, 47)	57 (53, 61)	54 (18, 90)	57 (51, 62)	72 (68, 75)	52 (51, 59)
p-value	0.046	0.016	0.029	0.077	0.270	0.007

Lifetime risk estimates represent the proportion of ATTICA cohort participants projected to encounter a fatal or nonfatal cardiovascular disease (CVD) event from the index age until the end of follow-up, assuming the final participant in the cohort was to reach the age of 85 years. The lifetime incidence rate, was computed utilizing adjusted life-table techniques as recommended by Kaplan and Meier. Modified life-table techniques were employed to consider the competing risk of mortality. Lifetime risks across different physical activity trajectories were compared using a two-tailed Z-test. 95% CI: 95% confidence interval; CVD: Cardiovascular disease.

of hypertension, hypercholesterolemia, and type II diabetes mellitus, and females who were consistently physically active had the lowest prevalence of obesity compared to the other physical activity groups ($p < 0.001$).

20-year incidence of cardiometabolic disorders in relation to trajectories of physical activity levels

The 20-year incidence rates of hypertension, hypercholesterolemia, and type II diabetes in both males and females, categorized by their physical activity trajectory, are presented in Table III. Individuals who maintained a sedentary lifestyle throughout the studied period demonstrated a significantly higher incidence of hypertension, regardless of sex ($p < 0.05$ for both sexes). Moreover, females who were consistently physically active showed a significantly lower incidence of hypercholesterolemia [Incidence Rate (95% Confidence Interval): 11 (4.2, 17.9) cases per 1,000 person-years], whereas those adhering to a sedentary lifestyle had higher incidence rates [Incidence Rate (95% Confidence Interval): 54.3 (33.1, 75.7) cases per 1,000 person-years]. Turning from physically inactive to active during the studied period also conferred a significant cardiometabolic protection, through lowering the incidence of hypertension and hypercholesterolemia ($p < 0.001$), as compared to those who were consistently inactive or turned from active to inactive (Tab. III).

Lifetime CVD risk in relation to trajectories of physical activity levels

The lifetime risk of CVD among males and females at three distinct index ages (40, 50, and 60 years old), categorized by their trajectories of physical activity levels is presented in Table IV. Among women aged 40 years old, those who maintained a sedentary lifestyle throughout the studied period had higher lifetime risk of CVD compared to their counterparts who consistently engaged in regular physical activity [51% (95%CI 45%, 57%) among consistently inactive females versus 45% (95%CI 43%, 57%) among consistently active females]. This disparity persisted at ages 50 and 60. Similarly, males who adhered to regular physical activity throughout the entire study duration exhibited a significantly reduced lifetime CVD risk compared to those adopting a sedentary lifestyle, particularly at the age of 60. This protective association of physical activity was apparent across all index ages (40 and 50 years old) as well.

Discussion

The present population-based study examined the trajectories of physical activity levels over a long-term period in relation to several demographic and clinical characteristics and health outcomes, of apparently healthy adults. A progressive decline in physical activity levels among both sexes was observed, as almost half of the cohort remained consistently inactive throughout the study period. Distinct patterns of physical activity trajectories emerged from our analysis, shedding light on the diverse pathways' individuals traverse in their physical activity behaviours. Profile analysis of those that were consistently inactive revealed that they had lower education and socio-economic status, but no other differences regarding their clinical status were observed. Furthermore, our study added to the compelling evidence of the impact of physical activity on cardiometabolic health across the lifespan. Participants who maintained a sedentary lifestyle throughout the study period had elevated lifetime CVD risk as compared to their consistently active counterparts.

Of the most important findings of our study is that almost half of the participants remained physically inactive through the entire 20-year studied period. This is in line with a body of previous research documenting in which a progressive decline in population physical activity levels over time has been reported. According to the World Health Organization, the latest global estimates show that 1.4 billion adults (*i.e.*, 27.5% of the world's adult population) do not meet the recommended level of physical activity to improve and protect their health [17]. Several longitudinal studies conducted in different regions around the world, have consistently reported similar to our findings, trends in reduced physical activity levels, in both adolescents and adults, illustrating the challenge of maintaining active lifestyles as individuals age [18, 19]. Specifically, the global age-standardized prevalence of insufficient physical activity was 23·4%, in men and 31·7%, in women [18]. The highest levels observed were in women in Latin America and the Caribbean (*i.e.*, 43·7%), south Asia (43·0%), and high-income Western countries (42·3%), whereas the lowest levels were in men from Oceania (12·3%), east and southeast Asia (17·6%), and sub-Saharan Africa (17·9%). Regarding younger people, globally, 81·0% of adolescents aged 11-17 years were insufficiently physically active (77·6% of boys and 84·7% of girls) [19].

Socio-demographic determinants in relation to physical activity trajectories

Our findings of socioeconomic disparities in physical activity trajectories resonates with a substantial body of existing literature documenting inequalities in activity levels among different socio-demographic groups [18-20]. In a global pooled analysis by Guthold et al., prevalence of inadequate physical activity was more than twice as high in high-income countries (36·8%) as in low-income countries (16·2%) [18]. Moreover, insufficient activity has increased in high-income countries during 2001-1016 (*i.e.*, 31·6 *vs* 36·8%). Concerning adolescents, the regions with the lowest prevalence were high-income western countries for boys (72·1%), and south Asia for girls (77·5%).

Numerous studies have highlighted the association between lower socioeconomic status and reduced engagement in physical activity, pointing to structural barriers, such as limited access to recreational facilities and resources as contributing factors [18-24]. In a large-scale epidemiological study in US, Wallace et al., examined how the rest-activity rhythms may mark development, aging, and physical and mental health in 12,526 participants from 3 to over 80 years old from the large-scale National Health and Nutrition Examination Survey (NHANES). They identified multiple trajectories of physical activity across adulthood, with factors such as age, sex, and socioeconomic status being as the most influential of these trajectories [21]. Stalling et al., analyzed data from 1507 participants (52.5% female), between 65-75 years old, residing in Germany, about physical activity participation (total, moderate and vigorous) and mean metabolic equivalents and found significant negative associations between physical activity and socioeconomic status [23]. In a review of Elhakeem et al. [24], the hypothesis that a lower childhood socioeconomic status is associated with less leisure-time physical activity during adulthood was strongly supported. All reviewed studies found that individuals with lower socioeconomic status were less likely to engage in leisure-time physical activity compared to those with higher socioeconomic status, even after accounting for individual-level factors. All these findings underscore the importance of considering the demographic dimension in interventions aimed at promoting active lifestyles and highlight the need for tailored approaches to address the diverse needs and preferences of various population groups.

Health-related outcomes in relation to physical activity trajectories

The link between physical activity and reduced CVD risk has been well-established in the literature through several studies [25-30]. In a previous analysis of our study it was revealed that participants being consistently physically active had lower CVD incidence during the 20-year follow-up period, as compared to those remained physically inactive or turned active/ inactive [11]. A recent harmonised meta-analysis by Paluch et al., highlighted that adding even 1000 steps a day were associated with a 10% reduction in the risk of CVD events [29]. The present analysis also revealed that adopting a physically active lifestyle during lifespan was associated with substantially lower burden of cardiometabolic disorders, *i.e.*, the development of hypertension, and hypercholesterolemia, as well as lower lifetime CVD risk, as compared to those remained or became physically inactive. These findings underscore the importance of promoting physical activity not only across all segments of the population, but also at any age, to effectively mitigate the lifetime burden of CVDs.

Potential mechanisms supporting the present findings

The observed associations between physical activity trajectories and CVD outcomes may be intermediated by various mechanistic pathways, as supported by extensive literature. Regular physical activity exerts beneficial effects on cardiovascular health through multiple physiological mechanisms, including improvements in lipid and triglycerides metabolism, blood pressure regulation, insulin sensitivity, and endothelial function. Additionally, physical activity enhances endothelial function by promoting nitric oxide production, leading to vasodilation and improved blood flow, thereby reducing hypertension, and enhancing vascular health [31-33]. Moreover, a plethora of research underscores the pivotal role of physical activity in glucose metabolism and insulin sensitivity, shedding light on its potential mechanisms [34]. Exercise stimulates glucose uptake by skeletal muscles, a process mediated by the translocation of glucose transporter proteins to the cell membrane, thereby lowering blood glucose levels and reducing the risk of insulin resistance and type II diabetes. A meta-analysis by Amanat et al., concluded that exercise interventions significantly improved glycaemic control and insulin sensitivity in individuals with type II diabetes [35]. However, in our study, none of the studied trajectories was associated with diabetes incidence, although, a clear trend towards engagement in physical activities was observed. This can be attributed in the relatively small number of people who developed diabetes during the studied period, lack of adequate confound, and not the absence of a true effect.

Furthermore, regular physical activity plays a crucial role in weight management and adiposity reduction, which are key factors in preventing metabolic disorders and reducing CVD risk. Exercise promotes energy expenditure, increases lean muscle mass, and decreases fat mass, thereby contributing to a healthy body composition and metabolic profile. Numerous studies have demonstrated the efficacy of exercise interventions in reducing visceral adiposity and improving cardio metabolic health outcomes [36, 37].

Limitations

The present study has several strengths, as it is one of the few in the literature that evaluated long-term trajectories of physical activity, their determinants, and relationships with cardiometabolic health, but also has several limitations that should be considered when interpreting the findings. The reliance on self-reported physical activity data through the International Physical Activity Questionnaire used may introduce recall bias and inaccuracies in assessing participants' true activity levels as compared to objective measures, like accelerometers; however, this tool has been found reliable and repeatable in previous studies and has been extensively used in epidemiologic assessment. Despite the efforts made, the dropout rate in follow-up examinations is significant (between 71 to 85%), but this is considered acceptable in epidemiological studies of long follow-up period, like the ATTICA study. Furthermore, the study took place only in Attica region, and therefore the homogeneity in terms of geographical location and ethnicity limits the generalizability of the findings to the broader Greek population, as well as other populations. However, it should be noted that in Attica region leaves 3,5 million people, *i.e.*, approximately 35% of the Greek population, in more than 50 urban and rural municipalities (including the capital city of Athens). Lastly, the inclusion of only baseline and follow-up assessments may not capture short-term fluctuations or intermittent changes in physical activity patterns and their impact on CVD outcomes.

Future research directions

Futur research in physical activity strategies could explore several key areas to further enhance our understanding and effectiveness in promoting physical activity. Investigate personalized approaches to physical activity promotion based on individual characteristics such as age, gender, fitness level, health status, and preferences. This could involve leveraging technology, such as wearable devices and mobile apps, to tailor interventions to individuals' needs and preferences. Moreover, future research could focus on the effectiveness of environmental and policy interventions in promoting physical activity at the community and population levels. This could include evaluating the impact of urban design, transportation policies, workplace wellness programs, and school-based interventions on physical activity levels. Sustainability in measures taken is a key for achieving good health. Future research should investigate strategies for promoting long-term maintenance of physical activity behaviors. Research could focus on identifying factors that contribute to sustained behavior change and developing interventions to support ongoing adherence to physical activity recommendations. An important issue is also to prioritize research on physical activity interventions that address health disparities and promote health equity. This could involve examining the effectiveness of interventions targeted towards underserved populations, including racial and ethnic minorities, low-income individuals, and people living in rural areas.

Conclusions

The findings of this comprehensive longitudinal study underscore the critical role of physical activity in shaping CVD outcomes over the lifespan. The present findings highlight the importance of promoting and sustaining regular physical activity throughout the lifespan, as well as for shaping targeted interventions, tailored to demographic and socioeconomic characteristics of the referent population. Tailored physical activity interventions addressing demographic and socioeconomic factors may help reducing the burden of CVD-related outcomes. These interventions should consider the accessibility of physical activity resources. This includes ensuring that affordable facilities are available in neighborhoods, as well as providing transportation options for those who may not have easy access. Addressing socioeconomic factors involves providing education about the importance of physical activity for preventing CVD and managing risk factors. This education should be accessible and understandable to people from diverse socioeconomic backgrounds.

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Conflict of interest statement

The authors declare no conflict of interest.

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Authors' contributions

ND, DP, TT: conceptualisation and writing the manuscript; TT: data analysis; ED, FB: investigation; DP, TT, YA, CT, ED: critical review of the manuscript; DP, CC, CP, CT, EL, PPS: methodology; DP: supervision and primary responsibility for final content. All authors have read and agreed to the published version of the manuscript.

Data availability statement

Data described in the manuscript, code book, and analytic code will be made available upon request to the corresponding author.

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