Original Research

Prevalence and Five-Year Incidence (2001-2006) of Cardiovascular Disease Risk Factors in a Greek Sample: The ATTICA Study

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Introduction: The purpose of this study was to evaluate changes in the prevalence of cardiovascular disease (CVD) risk factors in a population-based sample of Greek adults.

Methods: From May 2001 to December 2002, 1514 men and 1528 women (age >18 y), living in the Attica region of Greece, were enrolled in the ATTICA cohort study. In 2006, the 5-year follow up was performed (941 of the 3042 participants, 31%, were lost to follow up). The prevalence of hypertension, hypercholesterolemia, diabetes, obesity, smoking and physical inactivity, was assessed in both examinations through established procedures. Development of CVD (coronary heart disease, acute coronary syndromes, stroke, or other CVD) during the follow-up period was defined according to the WHO-ICD-10 criteria.

Results: During 2001-2006 there were 88 male and 102 female cases with hypertension per 1000 individuals, 237 male and 177 female cases with hypercholesterolemia per 1000 individuals, 58 male and 53 female cases with diabetes per 1000 individuals. In addition, 304 per 1000 males and 294 per 1000 females who were physically active at baseline examination became sedentary during the follow-up period. The prevalence of obesity reduced in males by 0.7% (p=0.66), but increased in females by 2.4% (p=0.10). Regarding smoking, its prevalence in 2001 was 47.2% in males and 39.6% in females; however, 27.5% of males and 24.5% of females stopped smoking, while 21.7% of males and 24.7% of females started smoking during the study period. The 5-year incidence of CVD was 11.0% in men and 6.1% in women (p<0.001); the case fatality rate was 1.6%.

Conclusions: The burden of CVD risk factors is increasing at alarming rates in the investigated population. Our data underline the need for immediate action from public health care professionals in order to control the upcoming epidemic.

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Cardiovascular disease (CVD) is one of the leading causes of death in both men and women in Greece, and is a major cause of death throughout the world.[1] Data from the Hellenic Statistical Service suggest that the number of deaths due to CVD increased from 14,603 per 100,000 in 1971 to 31,797 per 100,000 in 2001 (i.e. a relative increase of 117%) (Data from: www.statistics.gr, accessed on November 4, 2008). Moreover, during 1970-1990 Greece was the only country in the context of the European Union that showed an increase in mortality from coronary heart disease (CHD), although all-cause mortality was reduced and, as a result, life expectancy increased.[2] In a recent report from the 5-year follow-up (2001-2006) of the ATTICA Study, the age-adjusted annual incidence of CVD was 2.2% in men and 1.2% in women.[3] For comparison, the annual incidence of CVD in a Japanese study (i.e. a well-known low-risk population) was 2.1%,[4] while according to the National Health and Nutri-

tion Examination studies in US in the early 1990s (i.e. a moderate to high-risk population), the annual age-standardized CVD incidence rate was 2.25%.[5] These figures confirm the hypothesis that the Greek population is no longer a low-risk population for CVD, as it was in the 1950s or 1960s.

Several observational studies have shown that hypertension, diabetes, dyslipidemias, obesity, psychological disorders, unhealthy dietary habits, smoking and physical inactivity constitute the major risk factors for the development of CVD.[6] In 2006, the INTERHEART study investigators reported that abnormal lipids, smoking, hypertension, diabetes, abdominal obesity, psychosocial factors, consumption of fruits, vegetables, and alcohol, and regular physical activity, were the most significant factors associated with the risk of myocardial infarction worldwide, in both sexes and at all ages.[7] Measuring the prevalence of CVD risk factors at population level is essential in order to understand and better protect people's health status. Therefore, the EU, the European Society of Cardiology, the World Health Organization, the World Heart Federation and many other organizations support the development of local epidemiological studies in order to measure the levels and the secular trends of various health determinants. The prevalence of CVD risk factors in Greece has been mainly based on the findings from the Seven Countries study that started in the early 1960s,[8] and some more recent studies, such as the Athens Study in the 1980s,[9] the EPIC-Greek study in the 1990s,[10] and the ATTICA Study.[3]

Given that Greece has experienced marked, but uneven socioeconomic development during the past decades, with the average income increasing significantly, and taking into account the lack of data regarding the changes in the prevalence of CVD risk factors during the preceding years, in this study we aimed to present information about the major CVD risk factors, such as smoking, physical inactivity, hypertension, hypercholesterolemia, and diabetes, in a randomly selected, population-based sample from the Attica region. A secondary goal of this work is to perform a "validation" of the HellenicSCORE tool[11] (a calibration of the ESC SCORE project) that was developed based on local epidemiologic data to evaluate an individual's global CVD risk.

Methods

Baseline sampling procedure

The information presented is from the database of the ATTICA cohort study. The ATTICA study was carried out during 2001-2002, in the greater Athens area, i.e. the Attica region, which consisted of 78% urban and 22% rural areas. The sampling anticipated enrolling only one participant per household; it was random, multistage and based on the age (5 strata) and sex (2 strata) distribution of the Attica region (27 strata, census of 2001). First, an invitation was sent to 4056 inhabitants, based on the census roll of each city. People with a history of CVD were recorded (72 men, 45 women) and were then excluded from all further analyses. In addition, people who lived in institutions or had chronic viral infections did not participate in the sampling. Thus, 3042 CVD-free people participated in the study (75% participation rate); 1514 were men (age 18-87 years) and 1528 were women (age 18-89 years). All participants were interviewed by trained personnel (cardiologists, general practitioners, dieticians and nurses) who used a standard questionnaire.

The study was approved by the Bioethics Committee of Athens Medical School. Further details about the aims, design and methods used in the ATTICA Study may be found elsewhere in the literature.[12,13]

Baseline measurements

At baseline evaluation information about sociodemographic characteristics (i.e. age, sex, mean annual income in the previous year and years of school), history of hypertension, hypercholesterolemia and diabetes, family history of CVD, psychological information, dietary and other lifestyle habits, such as smoking status and physical activity, were collected. Socioeconomic status was defined using the years of school and the financial level of the participants. Smokers were defined as those who were currently smoking or had stopped smoking during the preceding year; the rest of the participants were defined as non-current smokers, and divided into never-smokers or former smokers. For the ascertainment of physical activity status the International Physical Activity Questionnaire was used (IPAQ[14]), as an index of weekly energy expenditure using frequency (times per week), duration (in minutes per time) and intensity of sports or other habits related to physical activity (in expended calories per time). Participants who did not report any physical activities were defined as physically inactive. Body mass index (BMI) was measured as weight (in kilograms) divided by standing height (in meters) squared, and obesity was defined as BMI

>29.9 kg/m^2. Arterial blood pressure (mean of 3 recordings) was measured at the end of the physical examination with the subject in a sitting position for about 30 minutes. Participants whose average blood pressure levels were ≥140/90 mmHg or were under antihypertensive medication were classified as having hypertension. Blood samples were collected from the antecubital vein between 8 to 10 a.m., in a sitting position after 12 hours of fasting and alcohol abstinence. Total serum cholesterol was measured using a chromatographic enzymic method in a Technicon automatic analyser RA-1000 (Dade Behring, Marburg, Germany) and hypercholesterolemia was defined as total cholesterol levels greater than 200 mg/dl or the use of lipid-lowering agents. The intra- and inter-assay coefficients of variation of cholesterol levels did not exceed 9%. Blood glucose levels (mg/dl) were measured with a Beckman Glucose Analyzer (Beckman Instruments, Fullerton, CA, USA) and diabetes mellitus (type 2) was defined according to the American Diabetes Association diagnostic criteria (i.e. blood glucose levels >125 mg/dl classified participants as having diabetes).

Table 1 gives the baseline socio-demographic information of the study's participants.

Table 1. Socio-demographic characteristics of the ATTICA study (baseline examination, 2001-02).

	Males	Females
N	1514	1528
Age (yrs)	45 ± 13	45 ± 14
Education status (years of school)	12.2 ± 3.7	11.9 ± 3.7
Uneducated (no school, %)	0.1%	0.4%
Annual income > €14,000.00	53.6%	37.5%
Unemployed (%)	1.0%	4.8%
Housekeeping (%)	0.4%	1.9%
Retired (%)	35.5%	35.7%

Follow-up procedure

During 2006, the 5-year follow up was performed. Of the 3042 initially enrolled participants, 2101 were found at follow-up examination (69% participation rate). Of the individuals that were lost to follow up (941), 706 were not found because of missing or wrong addresses and telephone numbers and 235 because they refused to be reexamined. Figure 1 illustrates the study's sample during the whole period. No significant differences in the baseline characteristics were observed between those who participated in the follow up and those who did not participate regarding the distribution of age (45 ± 14 vs. 45 ± 13 years, p=0.78), sex (males 50% vs. 50%, p=0.99), years of school (12.1 ± 4 vs. 12.0 ± 4, p=0.67), presence of hypertension (30% vs. 28%, p=0.12), diabetes (7% vs. 6%, p=0.27), hypercholesterolemia (39% vs. 33%, p=0.10), and obesity (19% vs. 15%, p=0.54). However, those who participated in the follow up were less likely to be smokers at baseline compared to those who were lost (41% vs. 49%, p<0.001). All participants were contacted through telephone calls (80% of the participants) or

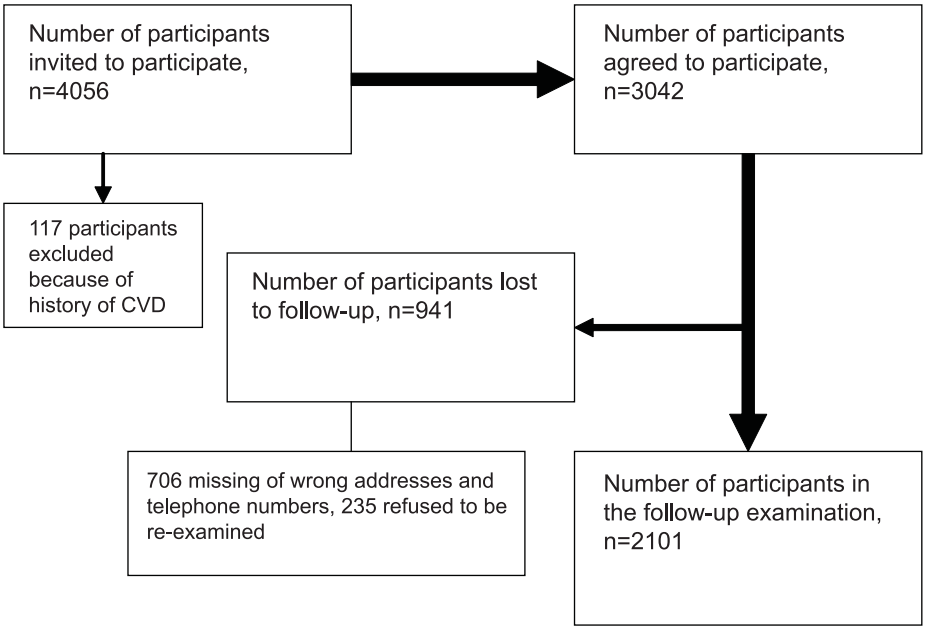

Figure 1. The ATTICA study sample. CVD – cardiovascular disease.

face-to-face interviews, when their telephone number was not available, and asked to provide all their medical records. The information assessed for the study population was as follows: (a) vital status (death from any cause or due to CVD); (b) development of CHD or stroke; (c) development of hypertension, hypercholesterolemia and diabetes (see baseline examination for definitions), as well as management of these conditions; (d) assessment of weight and height; and (f) lifestyle habits, including physical activity and smoking status.

Statistical analysis

Age-adjusted prevalence rates of the investigated CVD risk factors were calculated as the total number of cases of the specific condition at baseline and at follow-up examinations, divided by the number of individuals in the sample. At this point it should be noted that participants who were defined as hypertensive, hypercholesterolemic or diabetic at baseline examination were also considered as having the corresponding condition at follow-up examination. The latter classification was not used for current smoking habits, obesity status and physical inactivity. Incidence rates of CVD (using coding from the WHO-ICD 10th rev.) and the aforementioned risk factors were calculated as the ratio of new cases to the number of people who participated in the follow up and did not have this condition at baseline examination (no person-time was available for the investigated conditions).

The global CVD risk of the participants was calculated using the HellenicSCORE,[11] which estimated the 10-year risk for fatal CVD events based on age, sex, smoking habits, total serum cholesterol, and systolic blood pressure levels of the participants at baseline examination. Then, the values of the HellenicSCORE were categorized into seven classes and compared to the observed CVD event rates, in order to test the prognostic accuracy of the tool. Somer's d coefficient was then calculated to evaluate the association between the HellenicSCORE and the development of CVD events (values close to +1 indicate strong association).

Continuous variables are presented as mean values ± standard deviation and categorical variables are presented as frequencies. Differences between genders and the prevalence of risk factors were tested using the Z-test. Comparisons of mean values of normally distributed variables between males and females were performed using Student's t-test, after controlling for equality of variances using Levene's test, while for the continuous variables that were not normally distributed the Mann-Whitney non-parametric test was applied.

All reported p-values are based on two-sided tests and were compared to a significance level of 5%. SPSS version 14 (Statistical Package for Social Sciences, SPSS Inc, Chicago, IL, USA.) software was used for all the statistical calculations.

Results

Prevalence and 5-year incidence of CVD

At baseline evaluation (2001), 72 (4.7%) men and 45 (2.9%) women reported a history of CVD (p for gender difference <0.001). These participants were excluded from all further analyses. During the follow-up examination (2006) the prevalence of CVD had increased to 180 (15.2%) cases in men and 107 (9.2%) cases in women (p for gender difference <0.001). Thus, the 5-year incidence of CVD was 108 (11.0%) new cases in men and 62 (6.1%) new cases in women (p for gender difference <0.001). The overall 5-year CVD event rate was 170 cases (8.5%), while 32 of these events were fatal (21 men). Causes of death were myocardial infarction (25 cases), stroke (6 cases), and other CVD (1 case). Based on these figures, the annual incidence of CVD is 220 new cases per 10,000 men and 122 new cases per 10,000 women.

Prevalence of CVD risk factors in 2001 & 2006 examinations

In Table 2 the prevalence of hypertension, hypercholesterolemia, obesity, diabetes (type 2), smoking habits, and physical inactivity, at both baseline and follow-up examinations, are presented. During the 5-year period, the prevalence of hypertension, hypercholesterolemia, and diabetes increased in both males and females (p<0.01). Specifically, there were 8.8 new male and 10.2 new female cases with hypertension per 100 individuals (p for gender differences <0.001), 23.7 male and 17.7 female new cases with hypercholesterolemia per 100 individuals (p for gender differences <0.001), and 5.8 male and 5.3 female new cases with diabetes per 100 individuals (p for gender differences <0.001). The prevalence of obesity reduced in males by 0.7% (p=0.66), but increased in females by 2.4% (p=0.10). However, the prevalence of obesity is time dependent, thus incidence should be taken into account as a more accurate measure. The collected data showed that the overall 5-year incidence of obesi-

Table 2. Prevalence of cardiovascular risk factors (hypertension, hypercholesterolemia, diabetes, obesity, smoking and physical inactivity) in both baseline and follow-up examinations, and 5-year incidence of these conditions.

	Year of examination		5-year incidence
	2001	2006	2001-2006
Males			
Study participants, n	1514	1044	
Prevalence (%) of:			
Hypertension	36.6	46.5	8.8 per 100
Hypercholesterolemia	39.9	57.2	23.7 per 100
Diabetes	8.0	12.8	5.8 per 100
Obesity	20.8	20.1	21.8 per 100
Smoking (current)	47.2	38.9	16.8 per 100
Physical inactivity	58.7	69.0	30.4 per 100
Females			
Study participants, n	1528	1057	
Prevalence (%) of:			
Hypertension	23.7	34.0	10.2 per 100
Hypercholesterolemia	35.2	48.3	17.7 per 100
Diabetes	5.8	10.4	5.3 per 100
Obesity	15.9	18.3	11.9 per 100
Smoking	39.6	36.9	19.9 per 100
Physical inactivity	61.8	73.2	29.4 per 100

ty was 21.8% in men and 11.9% in women. Physical inactivity increased in both males and females by 10.3% and 11.4%, respectively ($p<0.01$), while 30.4 per 100 males and 29.4 per 100 females who were physically active at baseline examination became sedentary during the follow-up period. Regarding smoking habits, there was a reduction in current smoking in both genders, a finding that could have been biased by the large proportion of smokers lost to follow-up examination. However, further data analysis showed that 27.5% of males and 24.5% of females stopped smoking, while 21.7% of males and 24.7% of females started smoking during the study period.

The aforementioned changes in the prevalence of CVD risk factors were independent of the age of the participants, meaning that an increase was observed in all age groups. Moreover, stratified analysis by socioeconomic status showed that the low-educated and low-income participants were more likely to develop hypertension ($p<0.001$), hypercholesterolemia ($p<0.001$) and diabetes ($p=0.07$), compared to the high-educated and high-income. Moreover, low-educated and low-income participants had a higher prevalence of the CVD risk factors investigated compared to the high-educated and high-income people, in both examinations (data not presented here, all $p<0.05$). No associations between socioeconomic status and incidence of obesity, smoking habits and physical inactivity were observed ($p>0.3$ for all).

Prognostic accuracy of the HellenicSCORE

In Table 3 frequencies of CVD events by class of the HellenicSCORE are presented for both males and females. A progressive increase in the observed CVD event rate was found by HellenicSCORE class, in both males (Somer's $d=0.519$, $p<0.001$) and females (Somer's $d=0.702$, $p<0.001$), suggesting that the applied score is in agreement with the observed CVD events in the investigated sample.

Discussion

In this epidemiologic report the prevalence of CVD risk factors in two different examinations (i.e. 2001-

Table 3. Validation of the HellenicSCORE, which was used to assess the 10-year risk of fatal cardiovascular disease (CVD) events in the ATTICA sample.

Hellenic SCORE values (at 2001)	Development of CVD during 2001-2006 in males (%)	Development of CVD during 2001-2006 in females (%)
<1%	3.4	0.0
1-1.9%	10.4	2.2
2-2.9%	16.9	4.7
3-4.9%	19.5	3.7
5-9.9%	20.0	17.3
10-14%	29.0	38.9
>14%	48.6	-

2002 and 2006) of the ATTICA Study participants is presented, together with the 5-year incidence of CVD. Data analysis revealed that approximately 8.5% of the ATTICA study's participants developed a fatal or non-fatal CVD event during 2001-2006. Thus, the annual incidence rate was 220 per 10,000 men and 120 per 10,000 women, which means that about 550,000 people developed CVD during the preceding 5 years in Greece. However, it should be underlined that the extrapolation of these finding to the general Greek population should be done with caution, since the Attica region does not represent the whole country. Nevertheless, these figures underline the burden of CVD in a so-called "low-risk" population. Moreover, a considerable increase in the prevalence of all major CVD risk factors (i.e. hypertension, hypercholesterolemia, diabetes, obesity and physical inactivity) was observed, in both genders, and in all age groups.

Diabetes, hypertension and hypercholesterolemia constitute major clinical risk factors for the development of CVD. In the present study it was reported that the prevalence of these conditions increased substantially in all ages and in both genders. Specifically, regarding diabetes mellitus (type 2), an annual increase by 1% was evident in our cohort. Previous studies reported that the prevalence of the adult population with known diabetes increased from 250,000 in the mid 1970s[15] to 800,000 in the 2000s,[16] representing a three-fold increase in the diabetic population over the last three decades. These findings have many consequences, firstly, for individuals, by increasing their CVD risk and their disability level, which, as a result, affects their financial status and psychological well-being; and secondarily for their families, as well as for the health care system. Similar trends were observed regarding the prevalence of hypertension. Furthermore, regarding hypercholesterolemia, which has been strongly associated with the development of CVD,[17,18] the data presented indicate that the prevalence increased in males from 39.9% in 2001 to 57.2% in 2006 and in females from 35.2% in 2001 to 48.3% in 2006. Similarly, as in the case of diabetes and hypertension, the consequences of this increase are of considerable importance, at both individual and population level. Moreover, taking into account that although beneficial, the treatment of diabetes, hypertension and hypercholesterolemia is costly, further actions are needed from public health care authorities in order to prevent these upcoming epidemics in Greece.

Concerning obesity status, although the prevalence rates between the two examinations did not substantially differ, a 14% increase was observed in new cases of obesity, in both males and females. Obesity is now considered as a global epidemic, with harmful health, psychosocial and economic effects.[19] The increasing trends observed in Greece indicate a need for immediate and effective preventive measures, with high priority for those with metabolic risk factors.

Furthermore, physical inactivity showed a considerable increase in both men and women during the period 2001-2006, revealing that this unhealthy lifestyle behavior is spreading at an alarming rate in the Greek population. The benefits of physical activity for health have been underlined many years ago.[3] Several epidemiologic studies and clinical trials suggest that any type of physical activity reduces the risk of developing CVD, as well as various metabolic disorders, such as hypertension and diabetes. The data presented are of great importance, since knowledge of what determines physical activity changes during a short or a long period of time is necessary for the development of initiatives to raise and maintain a health enhancing level of physical activity within the population.

Concerning smoking habits, although the prevalence rates showed a constant or reducing situation, this is misleading because many smoker participants were lost to follow-up examination. Although a considerable proportion of people reported stopping smoking, the fact that about 22% of males and 25% of females started smoking during the studied period needs further and serious attention by the public heath authorities.

Finally, it was found that low-educated, low-income participants had a higher prevalence of the investigated CVD risk factors, as compared to the high-educated, high-income groups. Based on several observational studies, people's socioeconomic status, as determined by occupation, education level and income, has been related to all-cause mortality and morbidity.[20,21] Moreover, although at the beginning of the 20th century results from epidemiologic studies suggested that CVD was originally more common in the upper socioeconomic class than the lower or middle class, (i.e. a "disease of affluence"), this hypothesis seems to fail nowadays. Previous reports from the ATTICA study[22] underlined that the inverse relationship observed between education status and prevalence of CVD risk factors was mainly explained by the adoption of an unhealthy lifestyle, including smoking habits, physical inactivity, obesity and non-compliance with medication. The data presented underline

the need for special attention to be paid to people with a low socioeconomic status, in order to effectively reduce the burden of CVD in the future.

The mathematical prediction of future CVD events has received increased attention in recent years. The European Society of Cardiology published in 2003 a research project for the development of risk prediction charts based on data from 12 European cohort studies (the SCORE [Systematic Coronary Risk Estimation] project).[23] A clear suggestion was made by the project's investigators for the development of local scores. Thus, in 2007 the HellenicSCORE was developed based on a calibration of the ESC SCORE.[11] In this study an attempt was made to evaluate the prognostic accuracy of the HellenicSCORE against the observed CVD events in the 5-year follow up of the ATTICA Study. Data analysis revealed a very good classification of the HellenicSCORE as compared to the observed CVD events, in both males and females (Table 3). However, it should be noted that the HellenicSCORE predicts only future fatal events, while in the 5-year follow up of the ATTICA study the CVD event rate included both fatal and non-fatal events. Moreover, the SCORE has been developed to evaluate 10-year risk, while in this work only 5-year data were available.

Limitations

The present study had several strengths, presented above, but also had some limitations. First, the baseline and the follow-up examinations were performed once, and might be prone to measurement error. Thus, the prevalence of various clinical risk characteristics may have been overestimated. The date of the initiation of the development of hypertension, diabetes and hypercholesterolemia during the investigated period could not be recorded accurately. In addition, misreporting of physical activity status and smoking habits due to self-report may have misclassified the participants, and influenced, at least partly, the strength of the observed relationships. Somer's d, as well as other similar statistical tests, is weak in terms of prognostic accuracy; however, it is hard to apply other statistical methods because the HellenicSCORE evaluates CVD deaths, and in our case the number of deaths within the 5 year follow-up was rather small. Finally, the sample investigated was from a specific area, i.e. the Attica region, which does not represent the whole country The conclusions should therefore not be generalized to the total Greek population without reservations.

Conclusions

The burden of the major CVD risk factors, i.e. hypertension, hypercholesterolemia, diabetes, obesity, smoking and physical inactivity, is increasing at alarming rates in the sample of the Greek population we investigated. The presented findings underline the need for immediate action from public health care professionals in order to prevent the upcoming CVD epidemic that may cause serious problems to the health system and to the economy of the country.

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