

## Health Care Access and Prevalence of the Metabolic Syndrome Among Elders Living in High-Altitude Areas of the Mediterranean Islands: The MEDIS Study

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### ■ Abstract

**AIM:** The aim of the present work was to evaluate the relationships between sociodemographic, clinical, and lifestyle characteristics and the presence of metabolic syndrome, among high and low altitude living elderly individuals without known CVD. **METHODS:** During 2005-2011, 1959 elderly (aged 65 to 100 years) individuals from 13 Mediterranean islands were enrolled. Sociodemographic, clinical, and lifestyle factors were assessed using standard procedures. Metabolic syndrome was defined according to the (Adult Treatment Panel) ATP III criteria. Mountainous areas were defined those more than 400 meters in height. **RESULTS:** For the present analysis 713 men and 596 women were studied; the prevalence of the metabolic syndrome was 29% (24% in men, 35% in women,  $p < 0.001$ ). Furthermore, the prevalence of metabolic syndrome was 55% in the elders living in mountainous areas, as compared with 26% among those liv-

ing at sea-level ( $p = 0.01$ ). Similarly, the prevalence of hypertension, hypercholesterolemia, and obesity were higher in high altitude as compared with low altitude areas (all  $p$ -values  $< 0.01$ ). After adjusting for various confounders, elders living in high altitude areas were 3.06-times more likely to have the metabolic syndrome than those living at sea-level (OR = 3.06, 95%CI 2.02-4.65). However, when the annual number of visits to health care centers was taken into account, the effect of altitude of living was not associated with the presence of the syndrome. **CONCLUSIONS:** A considerable proportion of mountainous living elderly had the metabolic syndrome. Public health actions need to be taken to reduce the burden of cardiometabolic disorders by enabling better access to health care, especially in remote mountainous rural areas.

**Keywords:** diabetes · metabolic syndrome · elderly · high altitude · Mediterranean diet · interleukin 6

### Introduction

The metabolic syndrome is a cluster of cardiovascular disease risk factors, in particular hypertension, dyslipidemia, and hyperglycemia [1]. People suffering from the metabolic syndrome are at high risk of cardiovascular disease [2, 3]. The prevalence varies between populations,

with elderly people having the highest rates [2]. Recent studies from the Mediterranean areas reported over 25% prevalence among older individuals [4, 5]. Results from the Attica study reported 38% and 37% prevalence of metabolic syndrome in elderly males and females, respectively [6].

Living at high altitude has long been studied in relation to human health. It has been suggested

that high altitude can affect a range of diseases, either negatively (mainly circulatory or pulmonary disease) [7-8], or positively (diabetes and hypertension) [9]. A number of studies in different geographic areas (i.e., USA, Latin America, Asia, and Europe) investigated one or more cardiovascular disease (CVD) risk factors among high-altitude residents, but with controversial results. Some of these studies reported that the prevalence of hypertension at high-altitude residents was lower than in low-altitude ones [10-12]. Furthermore, cholesterol levels decreased with increasing altitude, whereas high-density lipoprotein cholesterol seemed to be increased [11, 13-16]. However, other studies reported opposite results, according to which high-altitude living was associated with elevated blood pressure and increased risk of atherosclerotic disease [17-19].

Until today, only one study from Peru has done research into the metabolic syndrome and has reported that the prevalence was higher, even though not significantly, in high-altitude residents compared to those living at low altitude [9]. In particular, no study so far has investigated access to health care, and considered this in relation to the prevalence of the metabolic syndrome in high- or low-altitude residents. Also, the aforementioned studies were conducted in mainland locations, with only one of them investigating the effects of altitude on health of older islander populations. However, this study was carried out in the population of the island of Crete, where the existence of the metabolic syndrome has already been reported in rural and mountainous populations [20]. The

prevalence has been attributed to the traditional Cretan lifestyle.

The increasing rates of the metabolic syndrome and the rapid changes in CVD mortality throughout the world are gradually becoming worse. Evidence suggests that the aging of the population is a central aspect in the prevalence of vascular diseases and mortality [21]. Given the lack of data, the aim of the present work was to find out whether there is an effect of altitude of living on the prevalence of the metabolic syndrome and its constituents among elders (> 65 years old) residing in various Mediterranean islands (i.e., Aegean islands, Crete, Ionian islands, Cyprus and Malta).

## Methods and participants

### *The study sample*

During 2005-2011, a population-based, multi-stage convenience sampling method was used to voluntarily enroll elders from the 13 Mediterranean islands: Malta (n = 250), Republic of Cyprus (n = 300) and the Greek islands of Mitilini (n = 142), Samothraki (n = 100), Cephalonia (n = 115), Crete (n = 131), Corfu (n = 149), Limnos (n = 150), Ikaria (n = 76), Syros (n = 151), Naxos (n = 145), Zakynthos (n = 103) and Salamina (n = 147).

For the present analysis, and since geographical data from Malta and Republic of Cyprus were not available, information from 713 men, aged  $74 \pm 7$  years and 596 women, aged  $73 \pm 7$  years was studied. Individuals were not included in the study if they resided in assisted-living centers, or had a clinical history of CVD or cancer, or if they had left the island for a considerable period of time during their life (i.e. >5 years). A group of health scientists (physicians, dietitians, public health nutritionists, and nurses) with experience in field investigation collected all the required information using a quantitative questionnaire and standard procedures.

The study followed the ethical considerations provided by the World Medical Association (52<sup>nd</sup> WMA General Assembly, Edinburgh, Scotland, October 2000). The Institutional Ethics Board of Harokopio University approved the study design (16/19-12-2006). Participants were informed about the aims and procedures of the study and gave their consent prior to being interviewed.

### *Evaluation of clinical characteristics*

All measurements performed in the different study centers were standardized. Weight and

#### **Abbreviations:**

BMI - body mass index  
 CI - confidence interval  
 CVD - cardiovascular disease  
 DBP - diastolic blood pressure  
 HEPA - health-enhancing physical activity  
 HDL - high-density lipoprotein  
 IPAQ - International Physical Activity Questionnaire  
 LDL - low-density lipoprotein  
 MEDIS - Mediterranean Islands Study  
 MET - metabolic equivalent of task  
 NCEP-ATP III - National Cholesterol Education Program Adult Treatment Panel III  
 OGTT - oral glucose tolerance test  
 OR - odds ratio  
 P-P plot - probability-probability plot  
 SBP - systolic blood pressure  
 SD - standard deviation  
 SPSS - statistical package for the social sciences  
 TC - total cholesterol  
 UN - United Nations  
 WMA - World Medical Association

height were measured using standard procedures to obtain body mass index (BMI) scores ( $\text{kg}/\text{m}^2$ ). Overweight was defined as BMI between 25 and  $29.9 \text{ kg}/\text{m}^2$ , while obesity was defined as  $\text{BMI} > 29.9 \text{ kg}/\text{m}^2$ . Waist circumference in cm was measured in the middle between the 12th rib and the iliac crest. Hip circumference in cm was measured around the buttocks. Central fat was defined as waist circumference greater than 102 cm for men and 88 cm for women. Diabetes mellitus (type 2) was determined by fasting plasma glucose tests in accordance to the American Diabetes Association diagnostic criteria:

- HbA1c  $> 6.5$  or
- fasting blood glucose  $> 125 \text{ mg}/\text{dl}$  or
- 2-h plasma glucose  $> 200 \text{ mg}/\text{dl}$  during an oral glucose tolerance test (OGTT) or
- a random plasma glucose  $> 200 \text{ mg}/\text{dl}$
- or they have been already diagnosed with diabetes.

Participants who had blood pressure levels  $\geq 140/90 \text{ mmHg}$ , or who used antihypertensive drugs, were classified as hypertensive. Fasting blood lipid levels were recorded as well. Hypercholesterolemia was defined by total serum cholesterol levels  $> 200 \text{ mg}/\text{dl}$  or the use of lipid-lowering agents according to the NCEP-ATP III guidelines [1]. HDL-, LDL-cholesterol and triglycerides were recorded. The coefficient of variation for the blood measurements was less than 5%. Finally, the metabolic syndrome was defined according to NCEP-ATP III criteria [1]. A diagnosis can be established if three or more of the following factors are present:

- waist circumference  $> 102 \text{ cm}$  (40 in) for men and  $> 88 \text{ cm}$  (37 in) for women,
- triglycerides  $> 150 \text{ mg}/\text{dl}$ ,
- HDL-cholesterol  $< 40 \text{ mg}/\text{dl}$  for men and  $< 50 \text{ mg}/\text{dl}$  for women,
- blood pressure  $> 130/ > 85 \text{ mmHg}$ ,
- fasting glucose  $> 110 \text{ mg}/\text{dl}$ .

### *Geographical evaluation*

Elsevier's dictionary of geography defines mountain as "a portion of the land surface rising considerable above the surrounding plains as elevated ranges, chains, massifs, plateaus" [22]. Accordingly, mountainous is an area where surface is steep and rough, with altitude higher than the surrounding areas. Although there is no standard definition for mountain environments, the absolute

elevation criterion is combined with other variables (e.g. the degree of the slope and the characteristics of the surrounding areas) to distinguish mountainous regions. The United Nations Environment Programme World Conservation Monitoring Centre adopted the lower limit of 300 meters for a high altitude area [23]. Alternatively, the lower limit has been set at 1000 meters at the equator, gradually decreasing to about 300 meters at the  $55^\circ$  of latitude. According to this definition, more than 2.2 million  $\text{km}^2$  in Europe is estimated as mountain area [24]. In this study, we considered all areas with elevation above 400 m as high altitude environments.

### *Evaluation of dietary habits, sociodemographic variables, lifestyle characteristics, and the health care system*

Dietary habits were assessed by a semi-quantitative, validated, and reproducible food-frequency questionnaire [25]. To evaluate the level of adherence to the Mediterranean diet, the Med-DietScore (possible range 0-55) was used [26]. Higher values for this diet score indicate greater adherence to the Mediterranean diet. Participants were encouraged to report the duration of their dietary habits (i.e. the number of years for which they had followed this dietary pattern).

Basic sociodemographic characteristics such as age, gender, annual income (basic annual income was defined as 8.000 euros per person according to the Greek Ministry of Economics), and lifestyle characteristics, such as smoking habits and physical activity status were recorded. Current smokers were defined as smokers at the time of the interview. Former smokers were defined as those who previously smoked, but had not done so for a year or more. The remaining participants were defined as occasional or non-current smokers. Physical activity was evaluated in metabolic equivalent of task (MET)-minutes per week, using the shortened, translated, and validated into Greek version of the self-reported International Physical Activity Questionnaire (IPAQ) [27]. Frequency (times per week), duration (minutes per session), and intensity of physical activity during sports, occupation, and/or leisure activities were assessed. Participants were instructed to report only episodes of activity lasting at least 10 minutes, since this is the minimum required to achieve health benefits. Minimally or health-enhancing physical activity (HEPA) active were defined those who reported at least 3 MET-minutes per week.

Moreover, the presence of small physicians' offices, health care centers, or hospitals in the area of living, and the annual number of visits for regular health status check-ups by the participants were recorded. Further details about the MEDIS study protocol may be found elsewhere [28].

### Statistical analysis

Continuous variables were presented as mean  $\pm$  standard deviation (SD), and categorical variables as frequencies. Comparisons of normally distributed continuous variables (i.e., age, school years, MedDietScore, body mass index, annual visits to health care centers) between groups were performed using Student's *t*-test. Spearman's rho coefficient was applied to evaluate the correlation between mean altitude of living and number of annual health care or hospital visits by a participant. Normality was tested using P-P plots. Independence between categorical variables was tested using the chi-square criterion. Additive logistic regression models were used to evaluate the association between presence of the metabolic syndrome and participants' characteristics (i.e., age, sex, high or low altitude area of residence, physical activity, adherence to the Mediterranean diet, smoking habits, years of education, living conditions, and annual visits to health care centers).

The results are expressed as odds ratios and 95% confidence intervals. Deviance residuals and Hosmer-Lemeshow criterion evaluated models' goodness-of-fit. A *p*-value  $< 0.05$  was considered to be statistically significant. SPSS software (version 18) was used for all calculations (SPSS Inc., Chicago, IL, USA).

## Results

### Lifestyle and area of living

The prevalence of the metabolic syndrome was 29% (i.e., 24% in men vs. 35% in women,  $p < 0.001$ ). Focusing on men and women living in high-altitude areas, the prevalence of the metabolic syndrome was 59% and 52%, respectively, while in participants living in low-altitude areas, the prevalence of the syndrome was much lower, namely 21% in men and 33% in women ( $p < 0.01$ ). Table 1 summarizes demographic, behavioral, and lifestyle characteristics of the sample, grouped by altitude of residence. Compared with elders living at low altitude, those living at high altitude were on average 3 years older and tended to be more physically active ( $p < 0.1$ ). Both groups had similar

**Table 1.** Demographic, behavioral, and lifestyle characteristics of MEDIS Study participants grouped by altitude of living, i.e., low or high altitude

Characteristic	Low altitude (n = 1102)	High altitude (n = 207)	p
Age (yr)	73.0 $\pm$ 7.0	76.0 $\pm$ 7.0	< 0.001
School years (yr)	6.6 $\pm$ 3.7	6.5 $\pm$ 2.9	NS
MedDietScore (0-55)	31.6 $\pm$ 4.0	31.7 $\pm$ 5.0	NS
Annual visits to health care centers (n)	4.7 $\pm$ 4.2	2.0 $\pm$ 1.1	0.002
AI > 8,000 euros (%)	19.5	21.5	NS
Current smoker (%)	21	14	0.02
Former smoker (%)	38	63	0.003
Min. or HEPA active (%)	41	48	NS
Living alone (%)	25	22	NS

**Legend:** Data are mean  $\pm$  SD, or percentage; *p*-values are derived using Student's *t*-test for normally distributed variables (age, school years, MedDietScore, annual visits to health centers), or Pearson's chi-square test for the categorical ones (annual income, current smoker, former smoker, minimally or HEPA active, living alone). AI: annual income. HEPA: health-enhancing physical activity. NS: not significant.

education and financial status. Moreover, no differences concerning the level of adherence to the Mediterranean diet was observed between elders living either low or high altitude. However, in high-altitude areas, the prevalence of current smoking was lower ( $p = 0.02$ ), and the prevalence of former smoking was higher ( $p = 0.003$ ).

Significantly, residents living in low-altitude areas visited health care centers or hospitals more frequently than those living in high-altitude areas ( $p = 0.002$ ). Also, health care centers and hospitals were found to be less well organized and physicians' offices tended to be smaller, in high-altitude than in low-altitude areas ( $p < 0.001$ ). Moreover, a strong inverse correlation was observed between altitude of living and the number of annual visits of elders to health care centers or hospitals for regular check-up ( $\rho = -0.67$ ,  $p < 0.001$ ).

### Clinical characteristics and area of living

Clinical characteristics and prevalence of the metabolic syndrome according to region of living are presented in Table 2. Elders living at high altitude had higher body mass index ( $p < 0.001$ ), higher prevalence of obesity ( $p < 0.001$ ), higher prevalence of hypercholesterolemia (total blood cholesterol levels  $> 200$  mg/dl) ( $p < 0.001$ ), hypertension ( $p < 0.001$ ), and consequently suffered from

**Table 2.** Clinical characteristics and prevalence of the metabolic syndrome in MEDIS Study participants grouped by altitude of living, i.e., low or high altitude

Characteristic	Low altitude (n = 1102)	High altitude (n = 207)	p
BMI (kg/m <sup>2</sup> )	27.9 ± 4.3	29.7 ± 4.3	< 0.001
Obesity* (%)	28	43	< 0.001
Central fat** (%)	85	71	0.009
Hypertension*** (%)	58	75	< 0.001
Diabetes* (%)	24	26	NS
Hypercholesterolemia# (%)	46	65	< 0.001
HDL-C <40mg/dl (%)	10	15	NS
TG >150mg/dl (%)	31	32	NS
Metabolic syndrome (%)	26	55	0.01

**Legend:** Data are mean ± SD, or percentage; p-values are derived using Student's *t*-test for the normally distributed variable (BMI), or Pearson's chi-square test for the categorical ones (central fat, obesity, hypertension, diabetes mellitus, hypercholesterolemia, metabolic syndrome, HDL-cholesterol levels <40mg/dl, triglyceride levels >150mg/dl). BMI: body mass index. HDL-C: high-density lipoprotein cholesterol. TG: triglycerides. NS: not significant. \* Obesity defined as BMI >29.9 kg/m<sup>2</sup>. \*\* Central fat defined as waist circumference >102/88 cm in men/women. \*\*\* Hypertension defined as systolic/diastolic blood pressure >140/90 mmHg. † Diabetes defined as fasting plasma glucose >125 mg/dl. # Hypercholesterolemia defined as total cholesterol >200 mg/dl.

metabolic syndrome (p = 0.01). Simultaneously, they had a lower prevalence of central fat (p = 0.009) than residents living at low-altitude. Older residents of both high- and low-altitude areas had almost similar prevalence of elevated triglycerides levels (>150 mg/dl) and low HDL-cholesterol levels (<40 mg/dl).

#### *Multi-adjusted analysis of the metabolic syndrome and area of living*

Age-sex only adjusted logistic regression analysis showed that people living at high altitude were 3.3-times more likely to have the metabolic syndrome compared with those living at low altitude (95% CI: 2.28-4.81). Every 100 m increase in the living height increased the likelihood of an elder having the metabolic syndrome by 22% (odds ratio per 100 m = 1.22, 95% CI: 1.10-1.34). Multiple logistic analyses were undertaken, as it was recognized that residual confounding may exist. The results are displayed in Table 3. A consistent relationship between living at high altitude and the likelihood of having the metabolic syndrome was

evident (**model 2** to **model 4**). Specifically, after adjusting for several confounders like physical activity and the adherence to the Mediterranean diet (**model 2**), smoking habits (**model 3**), and years of education and living conditions (**model 4**), data analysis confirmed that high-altitude living positively influenced elderly islanders to develop the metabolic syndrome.

When adjusting the latter model for the presence of health care centers, hospitals, or physician offices in the place of residence, the positive association of high altitude on the likelihood of having the metabolic syndrome remained significant (OR: 2.64, 95% CI: 1.73-4.03). However, when the annual number of visits to health care centers was taken into account, the effect of altitude of living no longer associated with the presence of the metabolic syndrome (**model 5**). Moreover, increasing age was associated with higher odds of the metabolic syndrome, whilst greater adherence to the Mediterranean diet seemed to offer some protection against the presence of the syndrome (**model 5**).

## Discussion

The present work showed that a considerable proportion of elderly participants have the metabolic syndrome, with those living at high altitudes appearing to have almost double the risk for the syndrome. Multi-adjusted analysis revealed that living at high altitudes in the studied Greek Mediterranean islands was associated with higher odds of the metabolic syndrome, irrespective of age, sex, education status, smoking, dietary habits, or physical activity. In addition, elders living at high altitude had higher prevalence of hypercholesterolemia, hypertension, and almost double the burden of obesity than residents in low-altitude (sea level) areas.

However, detailed analyses showed that the access to health care is the decisive parameter when studying the prevalence of the metabolic syndrome in the context of altitude of living. The association between living at high altitude and prevalence of the metabolic syndrome was not significant when the annual number of visits to health care centers was included in the analysis. Beside this important finding, it showed that the association remains significant when the mere presence of health care centers, physician offices, or hospitals were taken into account.

The confounding role of annual number of visits to health care centers on the relationship between

**Table 3.** Results from additive multiple logistic regression models performed to evaluate the association of various bio-clinical and lifestyle characteristics of the MEDIS study participants in relation to the metabolic syndrome (n=1209)

Characteristic	Model 1	Model 2	Model 3	Model 4	Model 5
Age (per 1 yr)	0.99 (0.97 - 1.01)	0.99 (0.99 - 1.01)	0.99 (0.97 - 1.02)	0.99 (0.97 - 1.01)	1.15 (1.03 - 1.29)
Gender (men vs. women)	0.62 (0.48 - 0.80)	0.64 (0.49 - 0.84)	0.62 (0.44 - 0.87)	0.61 (0.42 - 0.90)	0.20 (0.03 - 1.53)
High altitude area (Y/N)	3.31 (2.27 - 4.81)	3.34 (2.26 - 4.94)	3.26 (2.17 - 4.88)	3.06 (2.02 - 4.65)	1.76 (0.21 - 14.9)
Physical activity (Y/N)		0.68 (0.51 - 0.90)	0.68 (0.51 - 0.91)	0.81 (0.59 - 1.10)	1.80 (0.43 - 7.53)
MedDietScore (per 1/55)		1.02 (0.99 - 1.05)	1.02 (0.99 - 1.05)	1.02 (0.98 - 1.05)	0.82 (0.73 - 0.94)
Ever smoked (Y/N)			1.15 (0.80 - 1.64)	1.09 (0.74 - 1.62)	6.26 (0.99 - 39.4)
Years of school (per 1 yr)				0.96 (0.91 - 1.00)	1.09 (0.90 - 1.33)
Living alone (Y/N)				0.91 (0.64 - 1.29)	0.38 (0.08 - 1.89)
Annual visits in health care centers (per 1 visit)					1.17 (0.94 - 1.46)

**Legend:** Data are odds ratios (95% CI).

altitude and likelihood of metabolic syndrome could imply that it is not the altitude per se that contributes to the development of metabolic syndrome, but the lack of opportunity of access to health care for a better control of predisposing factors (blood pressure and lipids levels, weight control, etc). This is an important finding that has not been reported before in the context of the prevalence of the metabolic syndrome in relation to high-altitude living. Although the presence of health care units in the studied areas did not influence the relationship between altitude and the metabolic syndrome in our study, the supply of health care does not seem to be sufficient in high-altitude areas. The impact of medical care and control of risk factors on health status seem to be much greater than that of altitude of living.

In general, the prevalence of the metabolic syndrome of the studied elderly insular sample (i.e. 30%) was slightly higher than the prevalence of the syndrome in other recent studies conducted in the Mediterranean basin (i.e., around 25%) [4, 5]. Also, the prevalence was slightly lower than that of elders living in the metropolitan area of Greece, Attica [6]. Moreover, the observed higher prevalence of the metabolic syndrome in mountainous-living residents in the Mediterranean basin, as compared with low-altitude living ones, has been studied before only once in a Peruvian population, with similar prevalence of the syndrome among high and low altitude inhabitants (22% vs. 17%) [9]. However, before final conclusions are made, we need to be aware that the prevalence and the components of the metabolic syndrome are strongly influenced by age, sex, race, and ethnicity [29, 30].

To support the aforementioned findings, further analysis of the components of the metabolic syndrome and altitude of living was performed. The analysis revealed a higher prevalence of hypertension, obesity, and hypercholesterolemia in high-altitude living elders compared with those living in low-altitude areas. Despite the lack of previous findings regarding altitude and prevalence of the metabolic syndrome, a number of studies have already investigated cardiometabolic risk factors in different geographic areas worldwide, comparing high- vs. low-altitude adult residents, and showing similar results [8, 9, 11-19]. Some health conditions have been proposed to explain the accumulation of these metabolic risk factors among individuals living at high altitudes like acute mountain sickness, high-altitude pulmonary edema, high-altitude cerebral edema, hypoxia, lack of appetite, tiredness, stomach upset, and disinclination to work. The aforementioned conditions are assumed to result in physical restriction and mental depression, and consequently to promote the development of cardiometabolic disorders [7]. However, these health problems were observed at altitudes over 2500 m, while in our study the highest living altitude was only 800 m.

Rural areas have been associated with under-supply with health care services, an observation that was similar in the present analysis, where elders living in high-altitude areas were less likely to visit a health care center or a hospital for a regular health status check-up. In the majority of the studied islands, the capitals were located near the sea level, with good accessibility to health care services. In contrast, the higher altitude areas

were mainly rural, and the accessibility to the health care system was very difficult, especially in the winter time. This may explain why the relationship between altitude of living and metabolic syndrome was not significant anymore when the annual number of visits to health care centers was considered in the analysis. Haynes and Gayle studied the inequalities regarding deprivation and poor health, in rural areas of East Anglia, UK [31]. The inhabitants of remote areas, especially male elderly, seem to suffer from unemployment, poorer health due to social exclusion, geomorphologic difficulties deriving from poor access to health services, facilities, and social networks.

A recent study reported oversupply in health care and deficits in nursing and other health care personnel in Greece, with a higher number of physicians in the capital of Greece (i.e., Athens) and a lower number in other Greek regions (including insular rural areas) [32, 33]. Also, changes in the cardiometabolic profile of Cretan living in rural and mountainous areas have been reported during the past years [20, 34]. Recent analyses based on data from the same islands of the MEDIS study highlighted that primary and secondary health care services, together with nutritional services, could effectively reduce the burden of cardiometabolic risk factors among elders [35]. Thus, actions need to be taken in these directions to promote healthy living among elders, especially those living in rural areas and at high altitude. These findings are particularly relevant to current health care planners, since Greece and many other nations face a growing number of poor and underserved population.

This study has some limitations. It is a cross-sectional survey, and therefore faces a lack of causal relationships. Moreover, the altitude of living was not higher than 1000 m. Other studies that have investigated similar hypothesis considered altitudes of more than 2000 m. Therefore, the results are not fully comparable. However, in our study, the UN Environment Programme World Conservation Monitoring Centre definition of mountainous areas was adopted [23]. According to this definition, the mountainous population of the studied Mediterranean islands shares similar characteristics, and problems, with the mountainous areas investigated by others, and therefore, comparisons could be efficiently made.

## References

1. Executive Summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). *JAMA* 2001; 285:2486-2497.
2. Ford ES, Giles WH, Dietz WH. Prevalence of the meta-

## Conclusions

The prevalence of metabolic syndrome was high in the studied elderly insular population free of cardiovascular disease. The findings should be seriously taken into account by public health authorities to develop actions for reducing the burden of cardiometabolic diseases in this population, and consequently rescue financial "bleeding", especially under the spectrum of the recent economical crisis.

People living in high-altitude areas had a higher prevalence of the metabolic syndrome than those living in low-altitude areas, a fact that can be explained by the undersupply of adequate health care services in altitude areas. The latter underlines the need for immediate measures for health promotion among elders living in mountainous and rural areas. Health care and support, like local health care centers, continuous education regarding healthy living, e.g. by the organization of nutritional programs within the community, should be further extended [36].

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- bolic syndrome among US adults: findings from the third National Health and Nutrition Examination Survey. *JAMA* 2002. 287:356-359.
3. **Grundy SM.** Hypertriglyceridemia, atherogenic dyslipidemia, and the metabolic syndrome. *Am J Cardiol* 1998. 81:18B-25B.
  4. **Miccoli R, Bianchi C, Odoguardi L, Penno G, Caricato F, Giovannitti MG, Pucci L, Del Prato S.** Prevalence of the metabolic syndrome among Italian adults according to ATP III definition. *Nutr Metab Cardiovasc Dis* 2005.15(4):250-254.
  5. **Boronat M, Chirino R, Varillas VF, Saavedra P, Marrero D, Fábregas M, Nóvoa FJ.** Prevalence of the metabolic syndrome in the island of Gran Canaria: comparison of three major diagnostic proposals. *Diabet Med* 2005. 22(12):1751.
  6. **Panagiotakos DB, Pitsavos C, Chrysohoou C, Skoumas J, Tousoulis D, Toutouza M, Toutouzas P, Stefanadis C.** Impact of lifestyle habits on the prevalence of the metabolic syndrome among Greek adults from the ATTICA study. *Am Heart J* 2004. 147(1):106-112.
  7. **Peacock AJ.** Medical problems of high altitude. *J R Coll Physicians Edinb* 2008. 38:126-128.
  8. **Mohanna S, Baracco R, Seclen S.** Lipid profile, waist circumference, and body mass index in a high altitude population. *High Alt Med Biol* 2006. 7(3):245-255.
  9. **Baracco R, Mohanna S, Seclen S.** A comparison of the prevalence of metabolic syndrome and its components in high and low altitude populations in Peru. *Metab Syndr Relat Disord* 2007. 5(1):55-62.
  10. **Wolf EE, Selland MA, Mazzeo RS, Reeves JT.** Systemic hypertension at 4,300 m is related to sympathoadrenal activity. *J Appl Physiol* 1994. 76:1643-1650.
  11. **Fiori G, Faccini F, Pettener D, Rimondi A, Battistini N, Bedgoni G.** Relationships between blood pressure, anthropometric characteristic and blood lipid in high and low altitude population from central Asia. *Ann Hum Biol* 2000. 27:19-28.
  12. **Mirrahimov MM, Rafibekova ZH, Dzhumagulova AS, Meimanaliev TS, Murataliev TM, Shatemirova KK.** Prevalence and clinical peculiarities of essential hypertension in population living at high altitude. *Cor Vasa* 1985. 27:23-28.
  13. **Sharma S.** Clinical, biochemical, electrocardiographic and noninvasive hemodynamic assessment of cardiovascular status in natives at high to extreme altitudes (3000m-5500m) of the Himalayan region. *Indian Heart J* 1990. 42:375-379.
  14. **Fujimoto N, Matsubayashi K, Miyahara T, Murai A, Matsuda M, Shio H, Suzuki H, Kameyama M, Saito A, Shuping L.** The risk factors for ischemic heart disease in Tibetan highlanders. *Jpn Heart J* 1989. 30:27-34.
  15. **Dominguez Coello S, Cabrera De Leon A, Bosa Ojeda F, Perez Mendez LI, Diaz Gonzalez L, Aguirre-Jaime AJ.** High density lipoprotein cholesterol increases with living altitude. *Int J Epidemiol* 2000. 29:65-70.
  16. **De Mendoza S, Nuclete H, Ineichen E, Salazar E, Zerpa A, Glueck CJ.** Lipids and lipoproteins in subjects at 1,000 and 3,500 meter altitudes. *Arch Environ Health* 1979. 34:308-311.
  17. **Jefferson JA, Escudero E, Hurtado ME, Kelly JP, Swenson ER, Wener MH, Burnier M, Maillard M, Schreiner GF, Schoene RB, Hurtado A, Johnson RJ.** Hyperuricemia, hypertension, and proteinuria associated with high-altitude polycythemia. *Am J Kidney Dis* 2002. 39:1135-1142.
  18. **Pasini GF, Donato F, Buizza MA, Fantoni C, Gelatti U, Tani M, Grassi V.** Prevalence of risk factors for coronary heart disease in a mountain community in northern Italy. *G Ital Cardiol* 1999. 29:891-897.
  19. **Temte JL.** Elevation of serum cholesterol at high altitude and its relationship to hematocrit. *Wilderness Environ Med* 1996. 7:216-224.
  20. **Koutis AD, Lionis CD, Isacsson A, Jakobsson A, Fiores M, Lindholm LH.** Characteristics of the 'Metabolic Syndrome X' in a cardiovascular low risk population in Crete. *Eur Heart J* 1992. 13:865-871.
  21. **Mathers CD, Iburg KM, Salomon JA, Tandon A, Chatterji S, Ustun B, Murray CJ.** Global patterns of healthy life expectancy in the year 2002. *BMC Public Health* 2004. 4:66.
  22. **Kotlyakov VM, Komarova AI.** Elsevier's Dictionary of Geography. *Elsevier* 2007.
  23. **Kapos V, Rhind J, Edwards M, Price MF, Ravilious C.** Developing a map of the world's mountain forests. In: Price MF and Butt N. *Forests in Sustainable Mountain Development: A State-of-Knowledge Report for 2000*, CAB International 2000.
  24. **Hassan R, Scholes R, Ash N.** Ecosystems and human well-being: current state and trends: findings of the Condition and Trends Working Group of the Millennium Ecosystem Assessment. *Island Press* 2005. Chapter 1, pp. 681-716.
  25. **Tyrovolas S, Pounis G, Bountziouka V, Polychronopoulos E, Panagiotakos D.** Repeatability and validation of a short, semi-quantitative food frequency questionnaire designed for older adults living in Mediterranean areas: the MEDIS-FFQ. *J Nutr Gerontol Geriatr* 2010. 29(3):311-324.
  26. **Panagiotakos D, Pitsavos C, Stefanadis C.** Dietary patterns: a Mediterranean diet score and its relation to CVD risk and markers. *Nutr Metab Cardiovasc Dis* 2006. 16:559-568.
  27. **Papathanasiou G, Georgoudis G, Papandreou M, Spyropoulos P, Georgakopoulos D, Kalfakakou V, Evangelou A.** Reliability measures of the short International Physical Activity Questionnaire (IPAQ) in Greek young adults. *Hellenic J Cardiol* 2009. 50: 283-94.
  28. **Tyrovolas S, Zeimbekis A, Bountziouka V, Voutsas K, Pounis G, Papoutsou S, Metallinos G, Ladoukaki E, Polychronopoulos E, Lionis C, Panagiotakos DB.** Factors Associated with the Prevalence of Diabetes Mellitus Among Elderly Men and Women Living in Mediterranean Islands: The MEDIS Study. *Rev Diabet Stud* 2009. 6:54-63.
  29. **Kuk JL, Ardern CI.** Age and sex differences in the clustering of metabolic syndrome factors: association with mortality risk. *Diabetes Care* 2010. 33(11):2457-2461.
  30. **Prussian KH, Barksdale-Brown DJ, Dieckmann J.** Racial and Ethnic Differences in the Presentation of Metabolic Syndrome. *J Nurse Pract* 2007. 3(4):229-239.
  31. **Haynes R, Gale S.** Deprivation and poor health in rural areas: inequalities hidden by averages. *Health Place* 2000. 6:275-285.
  32. **Oikonomou N, Tountas Y.** Insufficient primary care services to the rural population of Greece. *Rural Remote Health* 2011. 11:1661.
  33. **Tountas Y, Karnaki P, Pavi E.** Reforming the reform: the Greek national health system in transition. *Health Policy*



2002. 62:15-29.
34. **Lionis CD, Sasarolis SM, Koutis AD, Antonakis NA, Benos A, Papavasiliou S, Fioretos M.** Measuring the prevalence of diabetes mellitus in a Greek primary health care district, *Fam Pract* 1996. 13(1):18-21.
35. **Tyrovolas S, Tountas Y, Polychronopoulos E, Panagiotakos D.** A parametric model of the role of nutritional services within the health care system, in relation to cardiovascular disease risk among older individuals. *Int J Cardiol* 2012. 155:110-114.
36. **Tyrovolas S, Polychronopoulos E, Tountas Y, Panagiotakos DB.** Modelling nutritional services in relation to the health status of older individuals living on Mediterranean islands. *Rural Remote Health* 2011. 11:1776.