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# Cardiovascular Risk Factors and Estimated 10-Year Risk of Fatal Cardiovascular Events Using Various Equations in Greeks With Metabolic Syndrome

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We investigated cardiovascular disease (CVD) risk factors in 1501 Greeks (613 men and 888 women, aged 40-65 years) referred to outpatients with metabolic syndrome (MetS) and without diabetes mellitus or CVD. The 10-year risk of fatal CVD events was calculated using European Society of Cardiology Systematic Coronary Risk Estimation (ESC SCORE), HellenicSCORE, and Framingham equations. Raised blood pressure (BP) and hypertriglyceridemia were more common in men (89.6% vs 84.2% and 86.8% vs 74.2%, respectively; $P < .001$). Low high-density lipoprotein cholesterol (HDL-C) and abdominal obesity were more common in women (58.2% vs 66.2% and 85.8% vs 97.1%, respectively; $P < .001$). The 10-year risk of fatal CVD events using HellenicSCORE was higher in men (6.3% $\pm$ 4.3% vs 2.7% $\pm$ 2.1%; $P < .001$). European Society of Cardiology Systematic Coronary Risk Estimation and Framingham yielded similar results. The risk equations gave similar assessments in a European Mediterranean population except for HellenicSCORE that calculated more MetS women requiring risk modification. This might justify local risk engine evaluation in event-based studies. (ClinicalTrials.gov ID: NCT00416741).

**Keywords:** epidemiology; cardiovascular disease; metabolic syndrome; gender; HellenicSCORE; ESC SCORE; Framingham

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## Introduction

The metabolic syndrome (MetS) is characterized by a clustering of cardiovascular disease (CVD) risk factors: disturbed glucose metabolism, abdominal obesity, hypertension, and dyslipidemia.[1] Different definitions have been proposed by the World Health Organization in 1998,[2] the National Cholesterol Education Program—Adult Treatment Panel III (NCEP ATP III) in 2001 (which were later modified by the American Heart Association in 2005),[3,4] and

the International Diabetes Federation in 2005.[5] The NCEP ATP III definition is considered by many investigators to be the most practical for clinical use.[6] Numerous studies have established that participants with MetS have a 3- to 4-fold increased risk of developing type 2 diabetes mellitus (T2DM),[6-8] and an almost 2-fold increased risk of the development of CVD, even after adjusting for traditional risk factors.[9-11] Metabolic syndrome is reaching epidemic proportions, paralleling the worldwide increase in obesity.[12] In the United States, MetS prevalence was estimated to be 22%, reaching 43% in those over 40 years of age.[13] European data suggest a prevalence of 15%,[14] while in Greece, the ATTICA study reported a prevalence of 25% among men and 15% among women,[15] and in the MetS-Greece study, the corresponding figures were 24% and 23%, respectively.[16]

It is important to stratify patients according to their risk and use this information as a guide for preventive treatment. The Framingham equation estimates the 10-year risk of developing coronary heart disease (CHD), CVD, and other cardiovascular endpoints. Beginning in the early 1950s, 5209 men and women aged between 30 and 62 years were recruited in the town of Framingham after the exclusion of CVD or other life-limiting diseases. Sex-specific prediction equations were formulated to predict the CHD risk according to age.[17,18] The Framingham model, however, has been shown to overestimate risk in Mediterranean countries with low CHD rates, such as Greece.[19] This problem was addressed by a prediction algorithm calibrated for European populations: the European Society of Cardiology Systematic Coronary Risk Estimation (ESC SCORE) project. The ESC SCORE project assembled a pooled data set of mostly population-based cohort studies from 12 European countries. A total of 205 000 individuals were included, 57% of which were men. A total of 8000 fatal cardiovascular events occurred during 3 000 000 person-years of observation.[20] This estimates the 10-year risk of fatal CVD and uses different charts for the low-risk populations of Southern Europe.[20] Although several studies have estimated the CVD risk of participants with MetS using risk models,[21,22] there are only a few data on the ESC SCORE algorithm.[23] Furthermore, there is the HellenicSCORE (Greek), based on ESC SCORE.[24] However, both a single country risk engine (HellenicSCORE) and the Framingham algorithm have never been compared with the ESC SCORE.

This study was undertaken to evaluate gender differences in CVD risk factor prevalence and estimated the 10-year risk of CVD fatal events in people with MetS in Greece using HellenicSCORE, ESC SCORE, and Framingham risk engines.

## Patients—Methods

### Study Sample

The current study is based on the baseline data of the Assessing the Treatment Effect in Metabolic Syndrome Without Perceptible diabeTes (ATTEMPT) study (ClinicalTrials.gov ID: NCT00416741). The study population consisted of a randomly selected sample of 2067 participants (846 males and 1221 females), recruited between 2005 and 2008, from all over Greece. The participants had attended outpatient clinics and practices and they met the NCEP ATP III diagnostic criteria (as modified by the American Heart Association)[4] for MetS. Specifically, at least 3 of the following factors should be present: waist circumference (WC) >102 cm for men or >88 cm for women; triglyceride (TG) levels >150 mg/dL (1.7 mmol/L); high-density lipoprotein cholesterol (HDL-C) levels <40 mg/dL (1.0 mmol/L) for men or <50 mg/dL (1.3 mmol/L) for women; blood pressure (BP) >130/85 mm Hg or treatment for these conditions and fasting glucose >100 mg/dL (5.6 mmol/L). However, for all analyses in the current study, only 1501 patients aged 40 to 65 years were included (613 males and 888 females), because both ESC SCORE and HellenicSCORE have not been validated for ages outside this range.

Exclusion criteria in our study were, TG levels >500 mg/dL (5.6 mmol/L), pregnancy or lactation, hormone replacement therapy, active hepatic disease (known hepatitis or unexplained persistent transaminases elevation >100 IU/L), secondary or resistant arterial hypertension, advanced renal disease (estimated glomerular filtration rate <60 mL/min/1.73 $m^2$) and the presence of CVD and/or DM (fasting plasma glucose $\geq$126 mg/dL [7 mmol/L], plasma glucose 2 hours after an oral glucose tolerance test $\geq$200 mg/dL [11.1 mmol/L], or antidiabetic drug therapy). These 2 last categories of patients are already at high risk and require a secondary prevention treatment strategy. Therefore, the study population constitutes a sample of individuals with the MetS who should be targeted for primary preventive measures.

### Investigated Parameters

Data collected from the study participants included a detailed personal medical history, measurements of the components of the MetS (blood lipids, BP, fasting glucose, WC), as well as other CVD risk factors (sex, age, body mass index [BMI], smoking status, and family history of premature CVD). Blood samples were collected from an antecubital vein between 8 and 10 AM, in a sitting position after a 12-hour fast. Biochemical evaluation was carried out in various laboratories that followed the criteria of the World Health Organization Lipid Reference Laboratories. All lipid tests were measured using enzymic methods adapted for automated analyzers.

Ten-year risk estimates for fatal CVD for each participant were calculated using the ESC SCORE risk model for low-risk populations[20] and the HellenicSCORE model, which is its calibration for the Greek population.[24] The ESC SCORE is the risk estimation tool endorsed by the ESC for the prediction of CVD mortality in European populations. This algorithm stratifies individuals as low (<1%), moderate (1%-4%), and high CVD risk (≥5%) individuals. Intensive risk factor management is recommended for participants at ≥5% risk.[25] Both the HellenicSCORE and the ESC SCORE take into consideration age, sex, systolic BP, total cholesterol, and smoking status. Furthermore, the 10-year risk of CVD death was also calculated by the Framingham risk model, which incorporates age, sex, BP, total cholesterol, HDL-C, history of DM, and smoking.[17,18]

The study protocol was approved by local and national ethics committees and written informed consent was obtained from each participant.

### Statistical Analysis

Continuous variables are presented as mean ± standard deviation (SD) or as median and interquartile range if the distribution was nonparametric. Qualitative variables are presented as relative frequencies. Risk scores are presented as median value and interquartile range. Associations between categorical variables were tested by the $\chi^2$ test. Comparisons between normally distributed continuous variables were performed by the Student *t* test. In the case of asymmetric continuous variables, the tested hypothesis was based on the Mann-Whitney test. We did 3 comparisons for risk calculations (HellenicSCORE, ESC SCORE, and Framingham). Therefore, according to the Bonferroni correction a *P* value of $<.05/3 = .017$ was considered significant.

The Kendall τ-b coefficient was computed to measure the concordance between the risk categories derived from the various risk models. Statistical package for the social sciences (SPSS) version 14.0 (SPSS Inc, Chicago, Illinois) software was used for all the calculations.

## Results

### Population Characteristics

Women with MetS were slightly older than men (mean difference 0.7 ± 0.3 years, $P < .04$). Moreover, women were less likely to be current smokers or have a family history of premature CVD, had a smaller WC, lower diastolic BP, lower TG levels, as well as lower glucose levels. Conversely, HDL-C was higher in women compared with men. No gender differences were observed regarding BMI, total cholesterol, low-density lipoprotein cholesterol (LDL-C), or systolic BP levels (Table 1).

### Prevalence of the MetS Components by Gender

Men were more likely to have hypertension and higher TGs, while women had a higher prevalence of low HDL-C and central obesity. There was no difference in the prevalence of impaired fasting glucose (fasting glucose >100 mg/dL [5.6 mmol/L]). Despite these findings, the total number of MetS criteria was equally distributed between the sexes; 34.4% men and 34.2% women had any 3 criteria, 40.8% and 38.9%, respectively, had 4 criteria and 25.8% and 26.9%, respectively, had all 5 MetS criteria (Table 2).

### Risk of Fatal Events

The 10-year risk of fatal CVD events, using the HellenicSCORE algorithm, was more than 2-fold higher in men than in women (6.3 ± 4.3% vs 2.7 ± 2.1%, $P < .001$). The corresponding risk using the ESC SCORE model was 5.8% ± 4.8% and 1.6% ± 1.4%, respectively ($P < .001$). Table 3 shows the various CVD risk categories calculated using each algorithm in men and women separately. The percentage of men assigned by HellenicSCORE to the high-risk categories (CVD risk ≥5%) was 3.8 times higher

**Table 1.** Demographic, Clinical, and biochemical characteristics of Participants With the Metabolic Syndrome[a]

| | Men | Women | *P* |
|---|---|---|---|
| N | 613 | 888 | |
| Age (years) | 54.1 ± 6.9 | 54.8 ± 6.3 | .04 |
| Body mass index (kg/m$^2$) | 31.4 ± 4.0 | 31.6 ± 5.1 | .49 |
| Smoking (%) | 40.9 | 22.0 | <.001 |
| Family history of CVD (%) | 40.9 | 34.7 | .01 |
| Waist (cm) | 105.1 ± 12.3 | 102.4 ± 11.1 | <.001 |
| SBP (mm Hg) | 143.3 ± 16.7 | 142.1 ± 17.4 | .17 |
| DBP (mm Hg) | 89.9 ± 10.5 | 86.9 ± 10.2 | <.001 |
| Total cholesterol (mg/dL) [mmol/L] | 257 ± 43 [6.64 ± 1.11] | 256 ± 42 [6.62 ± 1.08] | .7 |
| Triglycerides (mg/dL) [mmol/L] | 195 (167-261) [2.20 (1.88-2.95)] | 177 (141-216) [2.00 (1.59-2.44)] | <.001 |
| HDL-C (mg/dL) [mmol/L] | 40 ± 9 [1.03 ± 0.23] | 48 ± 11 [1.24 ± 0.28] | <.001 |
| LDL-C (mg/dL) [mmol/L] | 174 ± 42 [4.49 ± 1.08] | 171 ± 39 [4.42 ± 1.0] | .18 |
| Glucose (mg/dL) [mmol/L] | 105 ± 12 [5.84 ± 0.69] | 103 ± 11 [5.71 ± 0.62] | <.001 |

NOTES: CVD = cardiovascular disease; DBP = diastolic blood pressure; HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol; N = number; SBP = systolic blood pressure.
[a] Results are expressed as absolute number, mean SD or median, and interquartile range.

**Table 2.** Prevalence of the Various Criteria of the Metabolic Syndrome and Their Combinations in the Study Participants; Total Risk of Fatal Cardiovascular Disease, Calculated Using the HellenicSCORE, ESC SCORE, and Framingham Risk Models

| | Men | Women | *P* |
|---|---|---|---|
| N | 613 | 888 | |
| Hypertension (>130/85 mm Hg; %) | 89.6 | 84.2 | <.005 |
| Hypertriglyceridemia (≥150 mg/dL; %) | 86.8 | 74.2 | <.001 |
| Low HDL-C (<40 mg/dL in men and <50 mg/dL in women; %) | 58.2 | 66.2 | <.005 |
| Fasting glucose ≥100 mg/dL (%) | 71.9 | 70.9 | .68 |
| Central obesity (WC ≥102 cm in men and ≥88 cm in women; %) | 85.8 | 97.1 | <.001 |
| Any 3 criteria of MetS (%) | 33.4 | 34.2 | .78 |
| Any 4 criteria of MetS (%) | 40.8 | 38.9 | .45 |
| All 5 criteria of MetS (%) | 25.8 | 26.9 | .63 |
| HellenicSCORE 10-year risk of fatal CVD (%) | 6.3 ± 4.3 (5.4 [5.6]) | 2.7 ± 2.1 (2.0 [2.1]) | <.001 |
| ESC SCORE 10-year risk of fatal CVD (%) | 5.8 ± 4.8 (4.5 [5.1]) | 1.6 ± 1.4 (1.2 [1.6]) | <.001 |
| Framingham 10-year risk of CVD death (%) | 6.3 ± 4.6 (5.2 [6.0]) | 2.1 ± 1.8 (1.6 [2.1]) | <.001 |

NOTES: Risk scores are presented as mean ± standard deviation, as well as (median [interquartile range]). CVD = cardiovascular disease; ESC SCORE = European Society of Cardiology Systematic Coronary Risk Estimation; HDL-C = high-density lipoprotein cholesterol; MetS = metabolic syndrome; N = number; WC = waist circumference. To convert to mmol/L: divide HDL-C by 38.67, triglycerides by 88.57, and glucose by 18.

than the corresponding percentage of women (52.7% vs 13.7%, $P < .001$). Applying the ESC SCORE resulted in 44.8% of men versus 3.4% of women being assigned to the high-risk categories (ie, 13.2 times higher for men, $P < .001$). Moreover, using the ESC SCORE, 5.1% of men and 0.1% of women were assigned to a higher risk category than the category they would be in based on the HellenicSCORE, while 20.4% of men and 36.4% of women were assigned to a lower risk category (ie, underestimation of risk). Nevertheless, the overall concordance of the 2 models was quite good (Kendall τ coefficient was .767 for men and .596 for women, showing a highly significant correlation, $P < .001$). The 10-year Framingham-calculated risk of CVD death was also higher in men (6.3% ± 4.6% vs 2.1% ± 1.8%, $P < .001$); the percentage of men at ≥5% CVD death risk was 51.5% versus 7.7% among women ($P < .001$). When the Framingham was compared with the HellenicSCORE, 10.9% of men and 3.6% of women were assigned to a higher risk category and 14.4% of men and 24.5% of women to a lower risk category. However, the Kendall τ coefficient was relatively high (.756 for men and .621 for

**Table 3.** Cross-Tabulation of the Various Cardiovascular Risk Categories Calculated Using the HellenicSCORE and the ESC SCORE Algorithms in Men and Women

| | | Low (<1%) | Intermediate (1%-5%) | Increased (5%-10%) | Markedly increased (>10%) | Total for ESC SCORE |
|---|---|---|---|---|---|---|
| | | HellenicSCORE risk categories (men) | | | | |
| ESC SCORE risk categories (men) | Low (<1%) | 0% | 3.6% | 0% | 0% | 3.6% |
| | Intermediate (1%-5%) | 0% | 41.9% | 9.7% | 0% | 51.7% |
| | Increased (5%-10%) | 0% | 1.8% | 21.9% | 7.1% | 30.9% |
| | Markedly increased (>10%) | 0% | 0% | 3.3% | 10.6% | 13.9% |
| | Total for HellenicSCORE | 0% | 47.4% | 35.0% | 17.7% | |
| | | HellenicSCORE risk categories (women) | | | | |
| ESC SCORE risk categories (women) | Low (<1%) | 17.0% | 25.1% | 0% | 0% | 42.1% |
| | Intermediate (1%-5%) | 0% | 44.2% | 10.3% | 0% | 54.5% |
| | Increased (5%-10%) | 0% | 0.1% | 2.4% | 1,0% | 3.4% |
| | Markedly increased (>10%) | 0% | 0% | 0% | 0% | 0% |
| | Total for HellenicSCORE | 17.0% | 69.3% | 12.7% | 1.0% | |

NOTE: ESC SCORE = European Society of Cardiology Systematic Coronary Risk Estimation.

**Table 4.** Ten-Year Risk of Cardiovascular Death in Various Subgroups, as Calculated Using the ESC SCORE Algorithm

| | Men | Women | *P* |
|---|---|---|---|
| Smokers | 7.4 ± 6.0 (6.1 [6.4]) | 2.1 ± 1.8 (1.5 [1.9]) | <.001 |
| Non smokers | 4.6 ± 3.3 (4.0 [4.2]) | 1.5 ± 1.2 (1.1 [1.4]) | <.001 |
| Hypertensives (>130/85 mm Hg) | 6.0 ± 4.9 (4.7 [5.3]) | 1.7 ± 1.5 (1.3 [1.7]) | <.001 |
| Hypertriglyceridemics (≥150 mg/dL) | 5.7 ± 4.8 (4.4 [5.2]) | 1.6 ± 1.5 (1.2 [1.6]) | <.001 |
| Low HDL-C (<40 mg/dL in men and <50 mg/dL in women) | 6.0 ± 4.9 (4.7 [5.5]) | 1.5 ± 1.3 (1.1 [1.5]) | <.001 |
| Fasting glucose ≥100 mg/dL | 5.7 ± 5.1 (4.3 [4.9]) | 1.6 ± 1.4 (1.2 [1.6]) | <.001 |
| Centrally obese (WC ≥102 cm in men and ≥88 cm in women) | 5.7 ± 4.6 (4.6 [4.9]) | 1.6 ± 1.4 (1.2 [1.5]) | <.001 |
| Any 3 criteria of MetS | 5.4 ± 4.3 (4.2 [5.1]) | 1.5 ± 1.4 (1.1 [1.4]) | <.001 |
| Any 4 criteria of MetS | 5.7 ± 4.8 (4.5 [4.9]) | 1.5 ± 1.4 (1.2 [1.5]) | <.001 |
| All 5 criteria of MetS | 6.3 ± 5.2 (4.9 [5.4]) | 1.8 ± 1.5 (1.3 [1.8]) | <.001 |

NOTES: ESC SCORE = European Society of Cardiology Systematic Coronary Risk Estimation; HDL-C = high-density lipoprotein cholesterol; MetS = metabolic syndrome; WC = waist circumference. To convert to mmol/L: divide HDL-C by 38.67, triglycerides by 88.57, and glucose by 18.

women, $P < .001$), showing a good concordance between the 2 models. A further breakdown of the ESC SCORE-calculated risk for various subgroups (Table 4) shows a significant difference between men and women was observed in all categories, with the highest risk attributed to male smokers. From participants, 52.7% of all men with the MetS would receive intensive risk factor modification (increased and markedly increased risk) using the HellenicSCORE risk model, compared with 44.8% using the ESC SCORE and 51.5% using Framingham (analysis of variance [ANOVA] $P$ = not significant [NS]). The pattern for women was different, with 13.7% being considered at high risk using HellenicSCORE versus 3.4% with ESC SCORE ($P < .0001$) and 7.7% with Framingham ($P = .002$).

## Discussion

We found gender differences in the prevalence of MetS criteria. Increased BP and high TGs were more common in men, whereas low HDL-C and abdominal obesity were more common in women. Men were at a more than 2-fold 10-year risk of fatal CVD events compared with women, as shown by all 3 risk engines (HellenicSCORE, ESC SCORE, and Framingham). These risk engines demonstrated good agreement in classifying people into risk categories and predicting 10-year risk in men. However, HellenicSCORE revealed more women at higher risk and needing risk factor modification.

We showed that the relative contribution of various risk factors and the subsequent CVD risk

conferred by them to each sex differ significantly. Women with the MetS were older, but had a more favorable risk profile than men, with lower systolic BP, higher HDL-C (in absolute values), lower TGs and lower LDL-C, smoking less, and less often having a family history of CVD. Among the components of the MetS, high BP and higher TGs were the most common in men, whereas central obesity and high BP were the most important in women. This could reflect gender differences in the prevalence of CVD risk factors in the general population, as has already been reported in Greek epidemiological studies.[26]

Hypertension is generally less frequent in women than in men, owing perhaps to the beneficial effect of female sex hormones on the renin-angiotensin system (RAS),[27] differences in the endothelin pathway,[28] as well as other genetic factors.[29] The similar prevalence of hypertension in both sexes in our study could be attributed to the fact that our female cohort was older and had lost almost all the protective effects of estrogen.

Triglycerides are also influenced by sex hormones and are generally higher in men, whereas HDL-C is lower.[30] The different threshold for HDL-C led to more women fulfilling this diagnostic criterion of MetS.

The higher incidence of smoking in Greek men is well established, and although cigarette use among Greek women is rising, a recent study found that a difference of 23% still exists.[31] Furthermore, in our study, men were more likely to have a family history of CVD. This fits well with the general trend for higher risk in our male cohort and could possibly reflect an underlying genetic predisposition to acquiring MetS.

One major issue is central obesity and its contribution to CVD death risk. Part of this effect could be explained by the different thresholds used for defining the MetS in men and women (ie, the threshold for WC is 14 cm higher in men). The significance of central obesity in women with MetS has been noted in a Swedish study,[32] as well as the San Antonio Heart Study, which compared Caucasian Americans with Hispanic Americans.[33] A higher prevalence of the MetS was also observed in Spanish women than in men, mirroring the presence of a high WC.[23] The German Metabolic and Cardiovascular Risk Project (GEMCAS)[34] showed that abdominal obesity in adults attending a primary care physician is higher in women than in men (41.5% vs 36.4%, $P < .0001$). Although women were not more obese than men (in absolute terms) in our study, several were of older age, which is related with a greater tendency for a higher prevalence of abdominal (android) fat distribution.[35]

Few studies examined the prognostic value of the MetS gender-specific risks. A Spanish study found the ESC SCORE-calculated 10-year risk of participants with MetS (including patients with DM) to be 2.7%, significantly higher than that of control participants.[23] Men in the above mentioned study had a higher risk of CVD death than women (3.9% vs 1.9% using the ESC SCORE risk). Gender-related CVD risk of fatal events had a similar distribution but overall risk was quite lower than that seen in our study, reflecting perhaps the lower burden of CVD in the general population versus our patients who were referred to outpatient clinics. However, this Spanish study[23] had limitations. The definition of MetS used included abnormal glycemia >90 mg/dL and abdominal circumference $\geq$94 cm (men) or $\geq$80 cm (women). The participants were 60 $\pm$ 10 years old, but the calculating ability of ESC SCORE is for people 40 to 65 years old. Thus, a substantial number of patients were outside the reliable calculating range. The ESC SCORE for CVD mortality was compared with the Framingham score for CVD morbidity. Nevertheless, in this study (despite the lower threshold for abdominal obesity for both genders based on the International Diabetes Federation (IDF) MetS definition and the lower threshold for abnormal glycemia), women still had a higher prevalence of obesity but less than half the ESC SCORE risk of fatal CVD events than men. This might be because WC is not a parameter in the equations of existing CVD risk engines, including ESC SCORE. The Diabetes Epidemiology: Collaborative Analysis of Diagnostic Criteria in Europe (DECODE) study[36] enrolled a total of 2790 men without DM, aged 50 to 69 years from 7 population-based European cohorts, which were followed for CVD mortality over 10 years. The study showed that the predictive value of the WC was similar to that of the presence of the NCEP ATP III MetS. Thus, WC is a simple screening tool and it could be included as a risk factor in CVD risk scores.[36] In DECODE, among participants identified by the ESC SCORE risk as being at high fatal CVD risk, 6.1% died of CVD in contrast with the expected 5%.[36] Thus, ESC SCORE might underestimate real risk of fatal CVD events. This might be due, at least in part, to the absence of WC in the

ESC SCORE equation, although the prognostic impact of this additional risk factor on top of those included in the 3 risk algorithms has not been prospectively validated.

Our CVD risk findings in the 2 genders are in accordance with those of a study carried out in a Northern (ie, higher CVD risk) European country.[37] The GEMCAS project[37] used the ESC SCORE system to evaluate risk of fatal CVD events in 10 323 men and 18 852 women according to their WC. The study revealed substantial gender differences in risk of fatal CVD events in men than in women, both in participants with high and low WC. A higher proportion of women meeting the thresholds for abdominal obesity (WC > 88 cm) had a risk factor profile that was by far less severe than the corresponding male profile, necessitating different actions for the 2 genders.[37] This study was in agreement with data from the United States, where low WC in women was significantly correlated with low Framingham global risk.[37]

The ESC SCORE model has been incorporated into the Physicians Observational Work on Patient Education According to their Vascular Risk (POWER) study.[38] This study, with an estimated sample size of 60 000 patients, will determine if ESC SCORE can act as a suitable tool to aid the lowering of CVD risk.[38]

In the current study, a similar number of men with MetS would receive intensive risk factor modification using any of the 3 models. Despite the good Kendall τ coefficient between the 5 risk categories of the 3 risk engines, the consideration of the joined categories of high risk and very high risk (of practical interest) with HellenicSCORE versus the other 2 risk engines shows substantially more participants needing intensive risk factor modification than ESC SCORE and Framingham. The authors of HellenicSCORE have proposed that a slightly higher level of CVD risk could be expected in Greece compared with other low-risk countries, because of relatively high risk of stroke.[39] Nevertheless, local prospective data are needed to validate these HellenicSCORE findings.

If all the above are taken into consideration, the HellenicSCORE and the Framingham score can predict in a sufficient manner the risk of fatal CVD events in men comparable to that of (the low-risk version of the) ESC SCORE in a Mediterranean country, such as Greece, as it does in (high risk version for) Northern European populations.[40] However, HellenicSCORE showed a higher percentage of women at elevated or markedly elevated CVD risk that need intervention compared with the other 2 risk engines.

### Study Limitations

The study sample was not recruited from the general population, and our conclusions, therefore, may not be applicable at that level. However, this could be considered one of the study's strengths, as the population examined is that seen in everyday clinical practice. The risks of CVD fatal events presented here are estimates using the HellenicSCORE, ESC SCORE, and Framingham models and not observed events. They are, therefore, limited by the accuracy of the algorithms used, which, however, have been validated in various cohorts except for HellenicSCORE, which is relatively new. It should also be noted that the SCORE models do not incorporate HDL-C in their calculations, which could lead to underestimation of risk in some participants with MetS. However, the authors of the original SCORE model tested a system based on a total cholesterol/HDL-C ratio, which resulted in no advantage over the model using total cholesterol alone.[20] Another important limitation is the age range of our study sample. The SCORE algorithms have been designed for populations between 40 and 65 years of age, and Framingham for ages between 30 and 74. Thus, we were restricted to participants within this age range.

## Conclusions

We showed that the CVD risk factor profile of participants with MetS is differently distributed in men and women. Women were more likely to have central obesity and low HDL-C, whereas men were more likely to have hypertension and hypertriglyceridemia. We also showed that the risk in women is much lower than in men. A diagnosis of the MetS, therefore, carries a different significance for each gender. HellenicSCORE revealed more MetS women who need intensive risk factor modification. This might justify local risk engine development. This information requires verification by prospective studies but in the meantime it can be used to plan population-wide strategies for the prevention and treatment of MetS.

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