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ORIGINAL ARTICLE

C reactive protein and its determinants in healthy men and women from European regions at different risk of coronary disease: the IMMIDIET Project

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Summary. *Aim:* Differences in C-reactive protein (CRP) levels and its determinants in three European populations at different risk of coronary artery DISEASE (CAD) were studied. *Methods:* Subjects were recruited randomly in Limburg (Belgium), Abruzzo (Italy) and south-west (SW) London (England). *Results:* Ten-year risk of fatal coronary events (estimated using risk equations provided by the SCORE Project) was lower both in men and women from Abruzzo, intermediate in people from Limburg and higher in subjects from SW London. Within each country, high sensitivity (hs)-CRP levels were higher in the high-risk class in men but not in women. Men from Abruzzo had higher hs-CRP levels than those from Limburg and SW London. Women always had higher hs-CRP levels than men. The strongest hs-CRP determinant was body mass index (BMI, $R^2 = 0.14$) in women and waist circumference (WC, $R^2 = 0.046$) in men. The highest hs-CRP levels were observed in subjects with both high BMI and high WC. Metabolic syndrome was associated with high levels of CRP both in men and women, even after adjustment for confounders. *Discussion:* Difference in CRP levels cannot explain the European gradient of CVD risk, although CRP levels are associated with the calculated SCORE risk of fatal coronary events within each country.

Keywords: C reactive protein, coronary heart disease, metabolic syndrome, obesity, sex.

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Introduction

C reactive protein (CRP) is an acute phase marker whose blood levels depend on interleukin 6 and other inflammatory proteins that stimulate its production in hepatocytes, lymphocytes, alveolar macrophages and monocyte-derived macrophages in atherosclerotic plaques [1]. CRP, in turn, can induce a number of activities at the level of tissues and cells involved in the processes of atherosclerosis and thrombosis [2].

CRP has been considered an important cardiovascular risk factor both in healthy subjects [3] and in patients with coronary artery disease (CAD) [4]. However, the clinical predictive value of this protein is not fully established [5,6]. In the Reykjavik prospective study CRP is a relatively moderate predictor of CAD [7], while Ridker and co-workers showed that CRP has a strong predictive value and adds prognostic information to the Framingham risk score [8].

CRP levels are strongly associated with several risk factors for CAD [9,10]; therefore, it could be considered as a biological link between such conditions and CAD development. In particular, abdominal obesity has been reported repeatedly as a strong correlate of CRP levels [11–15].

The risk of CAD is differently distributed across Europe as age-standardized coronary event rates in both men and women

are lower in Mediterranean than in northern European countries. According to the MONICA data, such rates are about three times higher in the UK and twice higher in Belgium than in Italy [16]. Several factors may explain this gradient, mainly related to dietary and life-style habits and lipid levels. However, it is not known whether CRP levels and its determinants are different across European populations at different risk for CAD.

We set up a study to evaluate differences in the incidence of CAD risk factors in subjects from three European regions: Abruzzo (Italy), Limburg (Belgium) and SW London (England), which were considered to be at different risk of CAD (The IMMIDIET Project: Dietary Habit Profile in European Communities with Different Risk of Myocardial Infarction: the Impact of Migration as a Model of Gene-Environment Interaction, http://www.moli-sani.org/progetti/immidiet_site/welcome.html) [17].

In the framework of this study, the aim of the present report was to evaluate CRP levels and their metabolic determinants in men and women of three European regions to test whether they followed a similar European gradient as CAD risk profile.

Materials and methods

The IMMIDIET Project is a cross-sectional study of healthy male-female couples living together, randomly recruited from health assurance lists in the framework of three European general medical practices [18,19]. Recruitment took place in Limburg, a province in the Flemish part of Belgium, in Abruzzo, a region of southern Italy and in the south-west (SW) part of London, England. Abruzzo, Limburg and SW London were chosen as areas at lower, medium and higher CAD risk, according to MONICA data [16]. The recruitment strategies were carefully defined and standardized across the three recruiting centres. Subjects were examined in the framework of the practices, by research personnel who were accurately trained and followed well-standardized procedures.

Between October 2001 and October 2003, 1604 subjects (802 male-female couples), aged 25–74 years were enrolled in the study. The participation rate ranged between 70–90% in the different centres. Exclusion criteria for all groups were: history of cardiovascular disease, diabetes mellitus, familial hypercholesterolemia, malignancies, chronic diseases like heart, liver or renal failure, hypo/hyperthyroidism and epilepsy.

CRP was finally measured in 1466 (446 Abruzzo, 508 Limburg, 512 SW London) men and women. Subjects with hs-CRP >10 mg L^{-1} (5% Abruzzo, 6% Limburg, and 5% SW London) were excluded from the analysis to avoid introducing confounding due to acute or chronic inflammatory disease.

The study was approved by the ethical committees of all the participating institutions. All study participants agreed by written informed consent. Interviews were taken using a well-standardized questionnaire previously adopted in Italy [20] and translated into Flemish and English.

Blood pressure and anthropometric measurements

Blood pressure was measured with an automatic device (OMRON-HEM-705CP) [21]. Blood pressure (BP) values were recorded three times at the non-dominant arm and the last two values were taken as the BP. Measurements were performed in a quiet room with comfortable temperature, with the participants resting in a seated position for at least 5 min. Body weight and height were measured on a standard beam balance scale with an attached ruler, with subjects wearing no shoes and only light indoor clothing. Body mass index (BMI) was calculated as weight in kilograms divided by the square of the height in meters (kg m^{-2}). Waist circumference (WC) was measured according to the National Institutes of Health, National Heart, Lung and Blood Institute guidelines [22].

Biochemical measurements

Blood samples were obtained between 07.00 and 10.00 from patients who had been fasting overnight and had refrained from smoking for at least 6 h, by using a standard protocol in each study centre. Venous blood samples were obtained with minimum stasis using 21 gauge butterfly needles in K2 EDTA vacutainers. Blood was centrifuged within 3 h from the collection, plasma or serum were separated in 500 μL aliquots and immediately stored at −80 °C. Biochemical analyses were performed in centralized laboratories after shipping of aliquots in dry ice.

High sensitivity (hs)-CRP was measured in EDTA plasma samples in the Research Laboratory, Catholic University, Campobasso, Italy, within 12 months of collection. A latex particle enhanced immunoturbidimetric assay (IL Coagulation Systems on ACL9000, IL, Milan, Italy) was used. Quality control was maintained using in-house plasma pool and internal laboratory standard at 2.59 mg L^{-1} and 6.19 mg L^{-1}. Intra-day coefficient of variation (CV) was 3.3%, inter-day CV was 4.3%. The CVs for low and high hs-CRP control were 3.6% and 4.0% respectively.

Factor (F) VII:c levels were determined in citrated plasma, in the Centre for Molecular and Vascular Biology, Katholieke Universiteit Leuven, Belgium, with a one-stage clotting assay (FVII deficient plasma Hemoliance, Instrumentation Laboratory, Lexington MA, USA, and recombinant tissue factor based thromboplastin Innovin®, DadeBehring, Marburg, Germany).

Cholesterol, HDL-cholesterol, triglycerides and glucose were assessed in serum in the Unit of Epidemiology and Population Genetics, Institute of Food Sciences CNR, Avellino, Italy, by an automated analyzer (Roche Cobas Mira Plus, Roche Applied Science, Meylan, France). LDL-cholesterol was calculated according to the Friedewald formula [23].

Risk factors definition (see Supplementary material)

Fatal cardiovascular risks for each IMMIDIET subject were calculated applying the risk equations of the SCORE Project

[24]. Metabolic syndrome (MS) was defined according to the recent definition released by the IDF for Europid men and women [25]. According to CRP levels, participants were classified as being at low (CRP < 1.0 mg L^{-1}), medium (CRP 1.0 to 3.0 mg L^{-1}), or high risk (CRP > 3.0 mg L^{-1}) [26].

Statistical analysis

CRP, triglyceride and glucose levels were log transformed to normalize their positively skewed distribution. Multivariate association of study variables with country and sex was assessed modeling categorical data with procedure CATMOD in SAS, and continuous data with procedure GLM. Major determinants of CRP and interaction between major CRP determinants and sex were assessed applying multivariable linear regression analysis (Procedure REG in SAS), separately in men and women. The analysis strategy was as follows: (a) simple linear regression was used to identify variables associated with CRP levels at the level $P < 0.1$; (b) all the variables identified in the univariate analysis were inserted in a full model together with age and country; (c) because the inclusion of strongly correlated variables in the same regression model introduces collinearity problems, we checked for multicollinearity, measuring the variance inflation factor for each variable and the condition number for the full model. A variable whose variance inflation factor value is greater than 10 indicates the presence of collinearity; also, a large condition number, 10 or more, is an indication of the global instability of the regression coefficients. In a multivariate linear regression analysis in which all the aforementioned variables were included, no presence of collinearity was observed. In fact, the condition number was 5.0 for women and 4.3 for men, far away from the limit of 10. The variables with the largest values of variance inflation factor were BMI and waist circumference, but the values of the variance inflation factor were under the limit of 10 (variance inflation factor levels were lower than 4.5 both for BMI and waist, both in men and in women). We concluded that multicollinearity was absent or negligible in our data, and we constructed a multivariate model in which all the variables associated with CRP in univariate analysis were included.

Multivariate differences in the distribution of CRP by gender and countries were tested by analysis of the variance, together with Tukey test for multiple comparisons (Procedure GLM in SAS). All computations were carried out using the SAS statistical package (Version 8.2 for Windows; SAS Institute Inc., Cary, NC, USA; SAS Institute Inc., 1989).

Results

Men were older and more often smokers, and had higher systolic BP, diastolic BP, BMI, WC and glucose than women. Moreover, they showed higher values of plasma lipids, and lower HDL cholesterol levels (Table S1, Supplementary material).

The three populations differed for a number of variables, but not for age, systolic BP and WC in men and BMI and WC in women. In particular, subjects from Abruzzo were less active, more often smokers and had a lower socio-economic status than the other two populations (Table 1). In contrast, lipid levels were higher in people from Limburg.

Risk of fatal coronary events estimation and CRP

SCORE values were higher in subjects from SW London, medium in people from Limburg and lower in those from Abruzzo. In each country women had lower SCORE values than men (Table S2, Supplementary Material). CRP levels were significantly higher in the higher risk SCORE class in men, but not in women (Table 1). These associations were rather consistent among countries.

CRP determinants

Age, low socio-economic status, cigarette smoking, low HDL, high insulin level, and high BMI and WC in men and low socio-economic status, low physical activity, hypertension, low HDL, high triglycerides, insulin, FVII:c levels, and high BMI and WC in women were strongly positively associated with CRP levels in univariate analysis (Table 2). Menopausal status (incidence equal to 31%), oral contraceptive (68%) and hormonal

Table 1 C-reactive protein levels (mg L^{-1}) (geometric means and 95% confidence interval) according to the 10-year global risk of fatal coronary events (SCORE equations)

	Score			
	Low	Medium	High	*P**
Women				
Abruzzo (206)	1.27 (1.03–1.57)	1.58 (1.26–1.98)	1.91 (1.39–2.61)	0.094
Limburg (237)	1.11 (0.88–1.41)	1.22 (0.94–1.58)	1.21 (0.94–1.55)	0.85
SW London (245)	1.10 (0.86–1.42)	1.01 (0.82–1.23)	1.34 (1.13–1.60)	0.094
Total	1.17 (1.02–1.33)	1.23 (1.08–1.41)	1.37 (1.20–1.56)	0.24
Men				
Abruzzo (211)	1.11 (0.89–1.39)	1.18 (0.92–1.51)	1.95 (1.39–2.74)	0.020
Limburg (240)	0.61 (0.46–0.81)	0.90 (0.66–1.22)	1.14 (0.81–1.61)	0.020
SW London (241)	0.99 (0.72–1.36)	0.79 (0.62–1.01)	1.14 (0.95–1.37)	0.062
Total	0.84 (0.72–0.99)	0.94 (0.80–1.10)	1.24 (1.06–1.45)	0.0020

*Univariate analysis.

Table 2 Univariate and multivariate linear regression analysis of anthropometric, metabolic and coagulation correlates of C-reactive protein in men and women

Women (n = 623)				Men (n = 623)		
Variables	P*	P**	Partial R^2 (total = 0.233)	P*	P**	Partial R^2 (total = 0.084)
Age	0.25	–	–	0.0054	–	–
Socio-economic status	0.0001	0.094	–	0.0051	0.046	0.0061
Physical activity	0.0005	0.028	0.0070	0.098	0.41	–
Cigarettes	0.46	–	–	0.0003	0.0004	0.019
Hypertensive	< 0.001	0.59	0.0004	0.46	–	–
Cholesterol	0.86	–	–	0.97	–	–
LDL-cholesterol	0.63	–	–	0.093	0.17	–
HDL-cholesterol	0.0071	0.46	–	0.011	0.30	–
Triglycerides	< 0.0001	0.011	0.010	0.21	–	–
Glucose	0.63	–	–	0.098	0.51	–
FVII c	< 0.0001	< 0.0001	0.053	0.67	–	–
Insulin	< 0.0001	0.37	–	0.0068	0.62	–
BMI	< 0.0001	0.0040	0.14	< 0.0001	0.94	–
Waist circumference	< 0.0001	0.19	–	< 0.0001	< 0.0001	0.046

*Univariate analysis.
**Multivariate linear regression model adjusted for age, country and all non-redundant variables associated with CRP at univariate analysis with a $P < 0.1$.

replacement therapy (24%) were not associated with CRP levels in women (P = 0.12, 0.4 and 0.2, respectively).

In multivariate analysis, the strongest determinant of CRP levels was BMI (R^2 = 0.14) in women and WC (R^2 = 0.046) in men. Overall, the model explained 23.3% of total CRP variability in women and 8.4% in men. CRP levels were associated with BMI, FVII:c, triglycerides and physical activity in women and WC, cigarette smoking, socio-economic status and age in men (Table 2). CRP levels were higher in older men and smokers and subjects with low socio-economic status and increased with triglycerides, FVII, BMI and WC.

There was a significant interaction between gender and age ($P < 0.04$), cigarette smoking ($P < 0.01$), FVII:c ($P < 0.0001$) and triglycerides ($P < 0.0001$) in determining the levels of CRP.

Considering individual countries, CRP remained always associated with FVII:c and BMI in women and with WC in men (Table S3, Supplementary Material).

To better understand the relationship between obesity and CRP we evaluated the interaction between BMI and WC in determining CRP levels, by dividing these variables according to the median value in men and women (Fig. 1). Tertile subdivision was not possible due to the low numbers of subjects in each group. Both in men and women there was no interaction between BMI and WCs. In particular, in women the presence of both high BMI and high waist measurement significantly increased the levels of CRP as compared with having only high BMI or only high waist measurement.

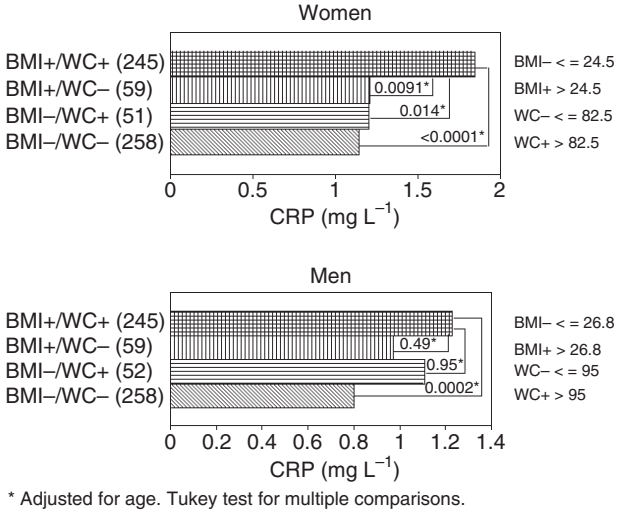

Fig. 1. Effect of body mass index and waist circumference on C-reactive protein levels.

CRP levels in countries

Using the AHA/CDC criteria, 23% of Abruzzo, 18% of Limburg and 16% of SW London women were classified as being at high risk (CRP > 3.0 mg L^{-1}) and 18%, 17% and 12% of men, respectively.

CRP levels varied significantly between countries after adjustment for age, in men and women. Subjects from Abruzzo had higher CRP levels than those from Limburg (P = 0.0002 in men and P = 0.024 in women) and SW London (P = 0.041 in men and P = 0.019 in women), while no differences were found between the last two populations (P = 0.22 in men and P = 0.99 in women). The observed difference in CRP levels across countries disappeared after further adjustment for covariates in women, but remained statistically significant in men (Table 3).

In each country CRP levels were higher in women than in men (Table 3), even after adjustment for confounders.

Table 3 C-reactive protein (CRP) levels by sex and country

CRP levels (mg L^{-1})	Men (n = 692)	Women (n = 688)	P (for sexes)
Abruzzo (n = 417)			
Median	1.48	1.59	
Range	0.71–2.46	0.76–2.87	
Geometric mean* (95% CI)	1.29 (1.08–1.53)	1.53 (1.32–1.78)	0.050*
Geometric mean** (95% CI)	1.19 (0.92–1.54)	1.41 (1.23–1.62)	0.003**
Limburg (n = 477)			
Median	0.87	1.39	
Range	0.48–2.11	0.56–2.62	
Geometric mean* (95% CI)	0.81 (0.69–0.94)	1.18 (1.04–1.34)	0.0017*
Geometric mean** (95% CI)	0.80 (0.61–1.03)	1.16 (1.04–1.31)	0.0007**
SW London (n = 486)			
Median	1.08	1.22	
Range	0.53–1.93	0.61–2.13	
Geometric mean* (95% CI)	0.97 (0.83–1.13)	1.17 (1.03–1.33)	0.046*
Geometric mean**(95% CI)	0.97 (0.75–1.27)	1.27 (1.13–1.42)	0.0004**
Comparisons among countries			
P*	0.0004	0.011	< 0.0001*
P multivariate**	0.0028	0.13	< 0.0001**

*Age adjusted.
**Adjusted for age, social status, cigarettes and waist in men and for age, physical activity, triglycerides, BMI and FVII:c in women.

Metabolic syndrome and CRP

Overall, 19% (n = 118) of men and 13% (n = 73) of women had MS according to the IDF definition for Europid populations. CRP levels were associated with the presence of MS, both in women and men, in univariate analysis and after adjustment for age and environmental risk factors (Table 4). Analysis across countries was not allowed, due to the low number of subjects with MS.

Discussion

As expected from the MONICA data on the rate of coronary events in European countries [16], the predicted risk at 10 years of fatal coronary events followed a north–south gradient, being lower in Italian subjects, intermediate in Belgians and higher in subjects living in England. We used the SCORE equations [24], a risk estimation system based on a large pool of representative European data sets, because it would capture the regional variation in risk, typical of the European population.

Table 4 C-reactive protein levels (mg L^{-1}) (geometric means and 95% confidence interval) in subjects with and without the metabolic syndrome (MS)

	MS			
	Yes	No	P*	P**
Women				
Abruzzo (206)	1.90 (1.17–6.66)	1.41 (1.08–4.11)	0.11	0.46
Limburg (237)	1.75 (1.22–5.75)	1.10 (1.08–3.01)	0.03	0.04
SW London (245)	2.14 (1.18–8.46)	1.07 (1.06–2.92)	0.0001	0.0005
Total	1.95 (1.11–7.05)	1.16 (1.04–3.19)	0.0001	0.0001
Men				
Abruzzo (211)	1.81 (1.38–2.37)	1.09 (0.92–1.30)	0.003	0.004
Limburg (240)	1.01 (1.24–2.74)	0.79 (1.11–2.19)	0.30	0.36
SW London (241)	1.02 (1.14–2.78)	0.99 (1.08–2.69)	0.82	0.90
Total	1.24 (1.03–1.49)	0.93 (0.84–1.03)	0.009	0.01

*P for metabolic syndrome in univariate analysis.
**P for metabolic syndrome adjusted for age, social status and cigarettes in men and for age, physical activity and FVII:c in women (triglycerides and waist circumference were not considered because included in the definition of MS).

While average CRP levels too were different in the three European populations, rather surprisingly such differences did not follow the expected gradient of fatal coronary events: CRP levels were indeed higher in Italian as compared with Belgian and English subjects, the latter being comparable. CRP levels were higher in women than in men, consistently in the three populations studied. These findings are in apparent contrast to the hypothesis that CRP levels are risk factors for CAD. Yarnell *et al*. [27] found significant differences in the levels of thrombotic and inflammatory markers, including hs-CRP, across 11 European MONICA centres. Cross-sectional correlations between populations showed that such factors and contemporary incidence rates for coronary events were generally weak and even inverse, as for CRP in women. Only fibrinogen, D-Dimer and von Willebrand factor showed significant correlations. Probably the latter, together with unmeasured environmental or genetic factors, could better explain the difference in risk between populations.

After adjustment for metabolic and anthropometric correlates, the difference in CRP levels among the three populations disappeared in women but not in men, suggesting a sexual dimorphism in the determinants of CRP. The difference in CRP levels between men and women remained significant even after adjustment for confounders, in agreement with other publications [28–31].

Again the latter finding is in contrast to the notion that CAD risk is lower in women and with our present data showing a risk of future fatal coronary events lower in women than in men in

all three countries studied. However, this difference was not present in other studies [14,15] and in particular when men and middle-aged women not taking hormone replacement therapy were compared [32].

When we analyzed how levels of CRP varied according to the predicted risk of future fatal coronary events, we found that they increased with the SCORE value in men but not in women in all populations studied. This suggests that CRP levels are associated with risk factors clustering in the high SCORE class.

Overall, a considerably higher percentage of CRP variability was explained by our model in women as compared with men. Moreover, interaction analysis showed that the associations between CRP levels and age, smoking habits, FVII and triglycerides were significantly different in men and women.

Significant age-sex interaction for CRP was also found in a population from central Italy [33]. The relation between age and CRP may have different causes in men and women, probably related to the influence of sex hormones on inflammatory markers [15]. However, in our study no association was found between CRP and either menopausal status, or use of oral contraceptive or hormone replacement therapy, probably due to lack of statistical power of subgroup analyses. Another CRP determinant in women but not in men was FVII, as also described by Woodward *et al.* [14].

The most important correlate of CRP was adiposity, a concept strongly supported by a recent systematic review, showing that weight loss was associated with an important reduction in CRP values [34].

Stratifying by gender, in agreement with Thorand *et al.* [15] we found that the strongest CRP determinant was BMI in women and waist circumference in men. These results confirm that the adiposity-mediated inflammatory response is different according to gender: inflammation depends more on total fat mass (of which BMI is an index) in women and more on visceral adiposity (waist measure) in men [13]. Moreover, only in premenopausal, but not in postmenopausal women or in men, did we observe an additive effect of BMI and WC in increasing CRP, further stressing the importance of sexual hormones in the association between CRP levels and obesity.

Evidence that CRP levels are associated with metabolic factors is also derived from our study on MS. MS [25] has been previously associated with the risk of cardiovascular disease and diabetes [35], as well as with high levels of CRP [36,37]. Consistently in our study, CRP levels were associated with MS in both sexes, both in univariate analysis and after adjustment for age and potentially confounding environmental factors.

We could not evaluate, due to our cross-sectional design, whether individuals with MS and increased CRP levels have an increased risk of future cardiovascular events as compared with patients with MS without increased CRP levels. However, in this case too, CRP would appear to be a possible link between metabolic conditions and coronary disease.

This study has several limitations. Its cross-sectional nature confines our analysis to observational data; therefore, no conclusion can be drawn on a possible cause–effect relationship. Additionally, the recruitment of the population, although randomly based, was limited to selected regions of Italy, Belgium and England. Caution should be used in extending our results to the general populations of these countries.

Because hard CAD endpoints were not measured in the present study, we used a prediction model as an index of the risk. We selected the SCORE model because it was the only model presently available comparing global risk estimation in different European countries, based on data originally derived from different European populations. However, results from the SCORE equation and their comparison among countries should be interpreted with caution, because this equation does not measure the risk of CAD but rather the risk of fatal CAD. This implies that different countries may have the same mortality rate but different incidences of disease, resulting in different case-fatality rates.

In conclusion, although CRP levels were associated with the calculated SCORE risk of fatal coronary events within each country, they cannot explain the European gradient of CVD risk. CRP levels were strongly dependent on metabolic factors and increased in subjects with MS, suggesting that CRP is an intermediate link between metabolic conditions and CAD. Sex differences in CRP associated with the SCORE risk and risk factor interactions require further study in larger data sets.

Authors' contributions

Individual contributions to the IMMIDIET Project and to the article are as follows. A. Arcari: concept of the study, analysis and interpretation of data, writing of the paper. F. Zito: recruitment of Italian and mixed Italian-Belgian couples, interpretation of the data. A. Di Castelnuovo: concept and design, management and statistics; writing of the paper. A. De Curtis: laboratory analysis, interpretation of the data. J. Arnout: member of the scientific committee of the project; concept and design, laboratory measurements. F. P. Cappuccio: member of the scientific committee of the project; concept and design, recruitment of English couples. M. de Lorgeril: member of the scientific committee of the project; concept and design, laboratory measurements. C. Dirckx: concept and design, recruitment of Belgian couples. V. Krogh: member of the scientific committee of the project; concept and design, nutrition epidemiology. A. Siani: member of the scientific committee of the project; concept and design, laboratory measurements. M. C. J. M. van Dongen: concept and design of the study, nutrition epidemiology. M. B. Donati: member of the scientific committee of the project; recruitment of Italian couples; interpretation of the data, writing of the paper. G. de Gaetano: concept and design of the study, interpretation of the data, writing of the paper. L. Iacoviello: project co-ordinator; concept and design, recruitment of Italian couples; laboratory measurements; interpretation of the data, data analysis; writing of the paper.

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Disclosure of Conflict of Interests

The authors state that they have no conflict of interests.

Appendix 1

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Supplementary Material

The following supplementary material is available for this article:

Table S1 Characteristics of study participants according to sex and country (Supplementary data).
Table S2 10-year global risk of fatal coronary events (*SCORE* equations) in men and women of the three studied populations (Supplementary data).
Table S3 Univariate and multivariate linear regression analysis of anthropometric, metabolic and coagulation correlates of CRP in men and women by country (Supplementary data).

This material is available as part of the online article from: http://www.blackwell-synergy.com/doi/abs/10.1111/j.1538-7836.2007.02851.x (This link will take you to the article abstract).

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