# Prevalence, awareness, treatment and control of hypertension in healthy unrelated male-female pairs of European regions: the dietary habit profile in European communities with different risk of myocardial infarction - the impact of migration as a model of gene-environment interaction project

Simona Costanzo<sup>a</sup>, Augusto Di Castelnuovo<sup>a</sup>, Francesco Zito<sup>a</sup>, Vittorio Krogh<sup>b</sup>, Alfonso Siani<sup>c</sup>, Jozef Arnout<sup>d</sup>, Francesco P. Cappuccio<sup>e</sup>, Michelle A. Miller<sup>e</sup>, Martien van Dongen<sup>f</sup>, Michel de Lorgeril<sup>g</sup>, Giovanni de Gaetano<sup>a</sup>, Maria Benedetta Donati<sup>a</sup>, Licia Iacoviello<sup>a</sup>, on behalf of the European Collaborative Group of the IMMIDIET project

Background Blood pressure control is of great importance in the prevention of cardiovascular events.

Aim To determine the prevalence, awareness, treatment and control of hypertension in healthy unrelated malefemale pairs of European regions.

Methods The dietary habit profile in European communities with different risk of myocardial infarction: the impact of migration as a model of gene-environment interaction (IMMIDIET) project was a cross-sectional study to investigate differences in the distribution of cardiovascular risk factors and dietary habits in healthy unrelated malefemale pairs married or living together in European regions. Eight hundred and two unrelated male-female pairs were randomly recruited in Abruzzo (Italy), Limburg (Belgium) and south-west London (England). Blood pressure was measured using an automated device. Hypertension was defined as systolic blood pressure of at least 140 mmHg or diastolic blood pressure of at least 90 mmHg or current antihypertensive treatment.

Results Overall, 24.4% of the population was hypertensive; among them, one-third was on antihypertensive treatment, but a significant proportion (56%) was unaware of the high blood pressure levels. Men were more often hypertensive than women (29.4 vs. 19.5%. P<0.0001). Women were more often treated than men (49.8 vs. 28.9%, P<0.0001). Women from south-west London showed blood pressure levels lower than those from Abruzzo and Limburg (P<0.001 for both, adjusted for age, BMI and social status). No difference among countries was found in blood pressure levels in men. The adjusted prevalence of hypertension was 20.8% in south-west London, 23.6% in Limburg and 28.87% in Abruzzo (Abruzzo vs. south-west London P = 0.005). The prevalence of antihypertensive treatment was 43.5, 42.5 and 32.1% in

Abruzzo, Limburg and south-west London, respectively. Out of those treated for hypertension, 42, 43 and 47.7% in Abruzzo, Limburg and south-west London, respectively, were well controlled.

Conclusion In communities of healthy unrelated malefemale pairs from three different European regions, more than half of hypertensive patients appeared to have blood pressure levels not at target values. Interventions are required to optimize the use and effectiveness of antihypertensive drug therapy in these patients. J Hypertens 26:2303-2311 © 2008 Wolters Kluwer Health | Lippincott Williams & Wilkins.

Journal of Hypertension 2008, 26:2303-2311

Keywords: antihypertensive therapy, awareness, blood pressure, Europe, hypertension

Abbreviations: ESH, European Society of Hypertension; HDL cholesterol, high-density lipoprotein cholesterol; hs-CRP, high sensitivity C reactive protein; 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 Project; LDL cholesterol, lowdensity lipoprotein cholesterol; MONICA study, MONItoring trends and determinants of CArdiovascular disease study; WHR, waist-to-hip ratio

<sup>a</sup>Laboratory of Genetic and Environmental Epidemiology, Research Laboratories, 'John Paul II' Center for High Technology Research, Care and Education in Biomedical Sciences, Catholic University, Campobasso, <sup>b</sup>Nutritional Epidemiology Unit, National Cancer Institute, Milan, <sup>c</sup>Unit of Epidemiology and Population Genetics, Institute of Food Sciences, CNR, Avellino, Italy, <sup>d</sup>Center for Molecular and Vascular Biology, Katholieke Universiteit Leuven, Leuven, Belgium, <sup>e</sup>Clinical Sciences Research Institute, Warwick Medical School, Coventry, United Kingdom, Department of Epidemiology, Maastricht University, Maastricht, The Netherlands and <sup>9</sup>Nutrition, Vieillissement et Maladies Cardiovasculaires, UFR de Médecine, Domaine de la Merci, La Tronche, France

Correspondence to Licia Iacoviello, MD, PhD, Laboratory of Genetic and Environmental Epidemiology, Research Laboratories, Center for High Technology Research and Education in Biomedical Sciences, Catholic University, Largo Gemelli 1, 86100 Campobasso, Italy Tel: +39 0874 312274; fax: +39 0874 312710; e-mail: licia.iacoviello@rm.unicatt.it

Received 14 May 2008 Revised 2 July 2008 Accepted 23 July 2008

### Introduction

More than a quarter of the world's adult population had hypertension in the year 2000, a proportion expected to increase to 29% (1.56 billion) by 2025. Men and women have a similar overall prevalence of hypertension, whereas it increases with age in all world regions consistently [1,2].

Hypertension is a major risk factor for coronary artery disease (CAD) [3,4]. Numerous epidemiological studies show that hypertension increases the risk of CAD not only in populations at risk but also in the general population. Because hypertension is one of the major modifiable risk factors for cardiovascular disease, its detection, treatment and control are important health objectives worldwide [5].

Randomized trials have shown that blood pressure (BP) lowering produces rapid reduction in cardiovascular risk that is highly consistent with prediction of risk reduction inferred from observational studies [6].

Unawareness, lack of treatment or undertreatment of hypertension is often observed in Western countries. The treatment and control of hypertension are usually more common in North America than in Europe [7]. Several epidemiological studies in European countries showed that individuals with well controlled BP represent a relatively small fraction of the overall hypertensive population, possibly because of inadequate treatment or noncompliance or both [7–12]. Men and women showed similar conditions with regard to the prevalence of awareness, treatment and control of hypertension, with a slightly lower prevalence in male individuals [7].

The dietary habit profile in European communities with different risk of myocardial infarction: the impact of migration as a model of gene-environment interaction (IMMIDIET) project (http://www.moli-sani.org/progetti/ immidietsite/welcome.html [13]) is a two-phase, population-based cross-sectional study funded by the European Union (EU) and performed by eight partners from seven sites in five EU countries. The first phase was designed to evaluate current dietary habits and metabolic risk profiles for cardiovascular disease of three European regions at different risk of myocardial infarction (MI) according to the MONItoring trends and determinants of CArdiovascular disease (MONICA) study results [14]. Abruzzo (Italy), Limburg (Belgium) and south-west London (England) were selected as European regions at low, medium and high risk for MI, respectively. Unrelated male-female pairs married or living together were recruited to better assess the role of environmental factors in cardiovascular disease. Indeed, (un)married couples allow the identification of determinants of diseases related to environmental or behavioral characteristics as compared with genetic components as pairs share the same lifestyle and socioeconomic environment but as a rule are genetically unrelated.

In the second phase of the project, we considered the historical post Second World War migration from Italy to Belgium as a 'natural' model to evaluate gene-environment interaction [13]. Individuals who had migrated to Belgium (Limburg) from southern Italy (Abruzzo) and integrated themselves within the Belgian culture (e.g. through marriage or living together), generated and shared a new lifestyle pattern different from that of either Italian couples living in Italy or Belgian couples living in Belgium. Therefore, individuals with a different genetic background, sharing the same environment, were compared among themselves and with individuals from the respective regions of origin, sharing the same environment and a similar genetic background. As indices of the MI metabolic risk profile, factors such as BP, which are likely to be under the combined influence of both dietary and genetic determinants, were investigated.

The aim of the present report was to assess the prevalence, awareness, treatment and control of hypertension in men and women of the three European communities in the framework of the first phase of the IMMIDIET project.

# **Methods**

# Study design

# Study participants

The IMMIDIET project and the recruitment of participants have been previously described in detail [15–17]. Briefly, this project compares healthy unrelated male–female pairs from regions of England, Belgium and Italy, including both urban and nonurban areas, in order to evaluate current dietary habits and risk profiles of the three communities. In each region, a local general practitioner (GP) network was established to recruit approximately 270 couples. Abruzzo, Limburg and south-west London were chosen as areas at lower, medium and higher MI risk, respectively, according to MONICA data [13].

Healthy pairs were unrelated male-female spouses or partners living together. To protect against selection bias, the selection of eligible pairs was randomized in each center. A computerized list of all eligible pairs in each practice was generated in advance, and an invitation was made by letter or phone call or both.

Participants were examined in the framework of the practices, by research personnel, who were accurately trained. Recruitment strategies were carefully defined and standardized across the three recruiting centers.

Between October 2001 and October 2003, 1604 participants (802 pairs) aged 26–65 years were enrolled. The participation rate ranged between 70 and 90% in the different centers. Exclusion criteria were a history of

cardiovascular disease, type 2 diabetes mellitus, familial hypercholesterolemia, malignancies, chronic diseases such as heart, liver or renal failure, hypothyroidism/ hyperthyroidism and epilepsy.

Interviews were performed using a well standardized questionnaire previously adopted in the Olivetti Prospective Heart Study [18].

The study was approved by the ethics committees of all participating institutions. All study participants agreed to participate by written informed consent.

#### Blood pressure and anthropometric measurements

Trained research personnel in the different centers of recruitment carried out BP and anthropometric measurements using methods that had been standardized beforehand during preliminary meetings in which all IMMIDIET consortium partners participated. BP was measured with an automated device (Omron-HEM-705CP, Omron Healthcare, Inc., Bannockburn, Illinois, USA) [19]. BP values were recorded three times on the nondominant arm, and the average of the last two values was 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 [20]. Body weight and height were measured on a standard beam balance scale with an attached ruler, with participants wearing no shoes and only light indoor clothing. BMI was calculated as weight in kilograms divided by the square of the height in meters (kg/m<sup>2</sup>). Waist and hip circumferences were measured according to the National Institutes of Health, National Heart, Lung, and Blood Institute guidelines [21] and waist-tohip ratio (WHR) was calculated.

# Definitions of hypertension, awareness, treatment and control of hypertension

Hypertension was defined as systolic BP (SBP) of at least 140 mmHg or diastolic BP (DBP) of at least 90 mmHg or current treatment with antihypertensive drugs in participants with a history of hypertension. Prehypertension [normal or high normal category of classification of BP levels according to European Society of Hypertension (ESH) guidelines 2007] was defined as SBP of 120-139 mmHg or DBP of 80-89 mmHg [22,23]. Optimal BP levels were defined as SBP less than 120 mmHg and DBP less than 80 mmHg [22].

Treatment (defined as current use of antihypertensive medication) was determined by direct documentation of all medications taken, monotherapy and combination therapy (more than one drug) was also considered. Awareness of hypertension was defined as answering 'yes' to the question 'have you ever been told that you had high BP?' Controlled hypertension was defined as treated hypertension with SBP less than 140 mmHg and DBP less than 90 mmHg [22,23].

### Definition of risk factors

Participants were classified as nonsmokers (if they had never smoked cigarettes), ex-smokers (if they had smoked cigarettes in the past) and current smokers (if they were currently smoking one or more cigarettes per day regularly). Overweight was defined as a BMI of at least 25 kg/m<sup>2</sup> and obesity as a BMI of at least 30 kg/m<sup>2</sup> in both men and women.

Social status was defined as a score based on two variables: education and job. Education was grouped in three categories: no education or primary school (i.e. less than 8-11 years of education, depending upon the country), which contributed zero points to the score of social status; secondary school (i.e. less than 13–16 years of education), which contributed one point to the score; and college/ university/higher level, which contributed two points to the score. Job was grouped in two categories: manual job, which contributed zero points to the score; and nonmanual job, which contributed one point to the score. Previous job was considered for retired participants. Finally, social status was defined as follow: 'high' if the score of social status was equal to or higher than three; 'middle' if the score was equal to two; and 'low' if the score was lower than two. Hypercholesterolemia was considered as a cholesterol level of at least 240 mg/dl or being on pharmacological treatment for hypercholesterolemia.

#### Biochemical measurements

Blood samples were obtained between 7.00 and 9.00 a.m. from patients who had been fasting overnight and had refrained from smoking for at least 6h. Blood samples were centrifuged, within 3 h, for 15 min at 3000 rpm.

Different biochemical analyses were centralized in different specialized laboratories from IMMIDIET partners after shipping the required aliquots in dry ice.

Measurements of serum lipids and blood glucose were performed by an automated analyser (Cobas-Mira-Plus, Roche, Milan, Italy). Low-density lipoprotein (LDL) cholesterol was estimated by the Friedwald formula: LDL cholesterol = total cholesterol - [high-density lipoprotein (HDL) cholesterol + triglycerides/5] [24].

High-sensitivity C reactive protein (hs-CRP) was measured in frozen plasma samples with a latex particle-enhanced immunoturbidimetric assay (IL Coagulation Systems on ACL9000, IL, Milan, Italy). A double quality control at 2.59 mg/l and 6.19 mg/l was used.

## Data analysis

Blood glucose, triglycerides and hs-CRP levels were log transformed to normalize their positively skewed

## **Results**

Baseline characteristics of women (n = 802) and men (n = 802) in the three populations are shown in Table 1. All environmental and metabolic risk factors were higher or more prevalent in men than in women.

## Mean blood pressure levels

The average mean BP (age, BMI, social status and region adjusted) was 128/81 mmHg in men and 118/76 mmHg in women. Men had higher BP levels than women in all three regions. Women from south-west London showed BP levels lower than those from Abruzzo and Limburg (P < 0.001 for both, adjusted for age, BMI and social status, Table 1). Average BP was 120/76 mmHg in Abruzzo, 118/75 mmHg in Limburg and 111/73 mmHg in south-west London. No difference among regions was found in SBP and DBP in men.

Both SBP and DBP increased with age in the total population and in both sexes (Fig. 1). SBP and DBP

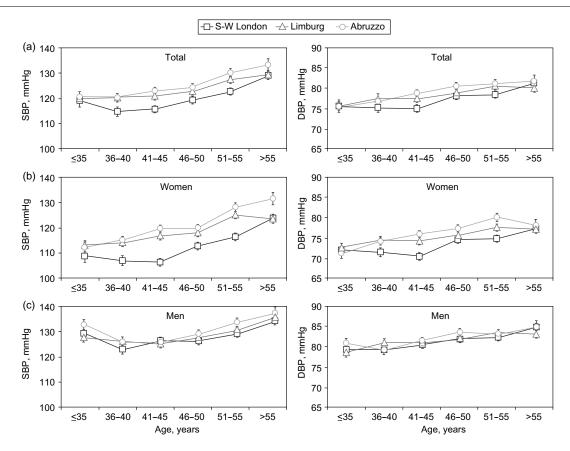
levels (adjusted for sex, BMI and social status) were lowest in south-west London, highest in Abruzzo and intermediate in Limburg (Fig. 1a). Significant differences (P < 0.05) were found at the 36–40, 41–45, 46–50 and 51–55 year ranges of age for SBP and the 41–45 and 51–55 year ranges of age for DBP between Abruzzo and south-west London participants and at the 36-40, 41-45 and 51-55 year ranges of age for SBP between Limburg and south-west London participants. No difference was found between Limburg and Abruzzo for both SBP and DBP. After stratification by sex, agespecific levels of SBP and DBP (adjusted for BMI and social status) were lowest in south-west London women. Significant differences (P < 0.05) were found at the 36– 40, 41–45, 46–50 and 51–55 year ranges of age for SBP and the 41-45 and 51-55 year ranges of age for DBP between Abruzzo and south-west London women and at the 36–40, 41–45 and 51–55 year ranges of age for SBP and the 41-45 year range of age for DBP between Limburg and south-west London women (Fig. 1b). In men, age-specific levels of SBP and DBP between Abruzzo, Limburg and south-west London were not significantly different (Fig. 1c).

After the exclusion of patients under treatment with antihypertensive drugs (9% of the sample), the positive correlation of SBP (r=0.22, P<0.0001, sex, BMI and social status adjusted) and DBP (r=0.18, P<0.0001, sex, BMI and social status adjusted) with age remained statistically significant, the slopes being not different among regions in the total population (SBP:  $\beta_{\text{south-west London}}$ =0.48  $\pm$ 0.09,  $\beta_{\text{Limburg}}$ =0.37  $\pm$ 0.08,  $\beta_{\text{Abruzzo}}$ =0.44  $\pm$ 0.09; DBP:  $\beta_{\text{south-west London}}$ =0.24  $\pm$ 0.05,  $\beta_{\text{Limburg}}$ =0.15  $\pm$ 0.04,  $\beta_{\text{Abruzzo}}$ =0.26  $\pm$ 0.06, 0.06, sex, BMI and social status adjusted) and after gender stratification (data not shown).

Table 1 Distribution of common risk factors for cardiovascular disease in English, Belgians and Italians by sex

	Women				Men				
Type of data and unit of measure	South-west London (n = 263)	Limburg ( <i>n</i> = 268)	Abruzzo ( <i>n</i> = 271)	P for region <sup>a</sup>	South-west London (n = 263)	Limburg ( <i>n</i> = 268)	Abruzzo (n = 271)	P for region <sup>a</sup>	P for sex <sup>b</sup>
Age, mean (SE) (years) Smoking habits, n (%)	47.3 (0.48)	45.2 (0.46)	42.3 (0.47)	<0.0001 <0.0001	48.8 (0.49)	47.4 (0.47)	46.2 (0.48)	0.0001 <0.0001	<0.0001 <0.0001
Never	172 (65)	139 (52)	181 (67)		150 (57)	90 (34)	103 (38)		
Current	31 (12)	63 (23)	64 (24)		44 (17)	72 (27)	102 (38)		
Former	60 (23)	66 (25)	26 (9)		69 (26)	106 (39)	66 (24)		
Social status, n (%)				< 0.0001				< 0.0001	0.02
Low	38 (14)	122 (46)	154 (57)		67 (26	112(42)	148 (55)		
Middle	136 (52)	46 (17)	84 (31)		82 (31)	60 (22)	77 (28)		
High	89 (34)	100 (37)	33 (12)		114 (43)	96 (36)	46 (17)		
SBP, mean (SE) (mmHg)	111.3 (0.98)	118.2 (0.92)	120.5 (0.97)	< 0.0001	128 (0.93)	129 (0.90)	130 (0.92)	_	< 0.0001
DBP, mean (SE) (mmHg)	72.8 (0.56)	75.3 (0.53)	76.3 (0.56)	< 0.0001	81.6 (0.58)	81.8 (0.56)	82.5 (0.58)	_	< 0.0001
Hypercholesterolemia, n (%)	50 (19)	95 (35)	45 (17)	<0.0001	77 (29)	115 (43)	72 (27)	<0.0001	0.02
BMI, mean (SE) (kg/m <sup>2</sup> )	25.8 (0.31)	25.5 (0.29)	26.4 (0.3)	_	27.2 (0.23)	26.7(0.22	27.8 (0.23)	0.004	< 0.0001
Glucose, median (Q1-Q3) (mg/dl)	84 (80-90)	76 (70–84)	73 (66–81)	< 0.0001	89 (84–97)	81 (74-87)	76 (69-85)	<0.0001	<0.0001

<sup>&</sup>lt;sup>a</sup> Adjusted for age, BMI, social status. (Only BMI and social status for comparison of age; only age and social status for comparison of BMI; only age and BMI for comparison of social status). <sup>b</sup> Adjusted for age, BMI, social status and region. (Only BMI, social status and region for comparison of age; only age, social status and region for comparison of BMI; only age, BMI and region for comparison of social status).



Systolic and diastolic blood pressure levels in south-west London, Limburg and Abruzzo populations by age group in the total population (a), women (b) and men (c). Values expressed as mean (standard error) are adjusted by sex, BMI and social status in the total population (a) and by BMI and social status in women (b) and men (c). DBP, diastolic blood pressure; SBP, systolic blood pressure.

# Prevalence of hypertension

The age, sex, BMI and social status-adjusted prevalence of hypertension was 20.8% in south-west London, 23.6% in Limburg and 28.8% in Abruzzo (Abruzzo vs. Limburg P = 0.07, Abruzzo vs. south-west London P = 0.005, south-west London vs. Limburg P = 0.4, Fig. 2). Hypertension was more prevalent in men than in women both in the whole sample (29.4 vs. 19.5%, age, BMI, social status and region-adjusted prevalence, P < 0.0001) and in southwest London (26.4 vs. 15.3%, P = 0.001) and Abruzzo (35.2) vs. 22.2%, P = 0.0001), whereas no difference was found in Limburg (26.5 vs. 20.8%, P = 0.09) (Fig. 2).

Abruzzo men had a higher prevalence of hypertension than those from south-west London and Limburg (P=0.01). Prehypertension prevalence was higher in Abruzzo than in south-west London women (32 vs. 19%, respectively, P = 0.001). Concerning optimal BP levels, women from Abruzzo showed a lower prevalence (45.5%) than those from Limburg (53.5%, P = 0.04) and south-west London (66.2%, P < 0.001, adjusted for age, BMI and social status, Fig. 2). A lower prevalence of optimal BP levels was also found in south-west London

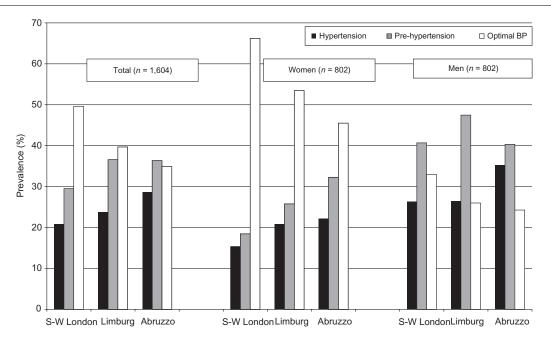
and Abruzzo men (33 vs. 24.3%, respectively, P < 0.025, adjusted for age, BMI and social status, Fig. 2).

After stratification for sex and adjustment for age, social status and region, hypertensive women showed BMI, triglyceride, glucose and hs-CRP levels higher than nonhypertensive women, whereas BMI, WHR and HDL cholesterol levels were higher in hypertensive men than in nonhypertensive men (Table 2).

#### Hypertension awareness, treatment and control

Twelve percent of persons declared having high BP, 1% ignored the BP values, whereas 87% denied having high BP. Only 46.2% of the latter had measured levels of BP that were optimal according to the definition of the ESH guidelines 2007 (south-west London, 55.1%; Limburg, 45.2%; Abruzzo, 39.8%; age, sex, BMI and social statusadjusted prevalence, P < 0.0001), whereas 38.2% had prehypertensive levels of BP (south-west London, 31.2%; Limburg, 41.5%; Abruzzo, 41.8%; age, sex, BMI and social status-adjusted prevalence, P = 0.0009) and 15.6% had hypertensive levels of BP (south-west London, 13.7%; Limburg, 13.4%; Abruzzo, 18.3%;

Fig. 2



Age, BMI and social status-adjusted prevalence of hypertension in south-west London, Limburg and Abruzzo in the total population and in women and men. BP, blood pressure.

age, sex, BMI and social status-adjusted prevalence, P = 0.06).

A significant proportion (56%) of participants with high measured levels of BP were unaware of their BP levels, with a male predominance (60.7 vs. 43.9%, age, BMI, social status and region-adjusted prevalence, P = 0.001). No significant differences among regions were found (Table 3).

Only 36.5% of the overall hypertensive patients received regular pharmacological treatment; the percentage of patients receiving treatment was lower in south-west London (32.1%) than in Abruzzo (43.5%) and Limburg (42.5%). Hypertension treatment in men was lower than

in women, both in the whole population (28.9 vs. 49.8%, age, BMI, social status and region-adjusted prevalence, P < 0.0001) and in each region (Table 3). Forty-six percent of treated patients received a single drug therapy; the most commonly used drugs in monotherapy were βblockers (40.9%), angiotensin-converting enzyme inhibitors (21.2%) and diuretics (16.7%), followed by calcium channel antagonists (12.1%) and angiotensin II receptor blockers (7.6%). Treated Italian hypertensive patients were more often under combined therapy (75.2%, age, sex, BMI and social status-adjusted prevalence) than Belgian (36.6%, age, sex, BMI and social status-adjusted prevalence, Abruzzo vs. Limburg P = 0.0002) and English (41.4%, age, sex, BMI and social status-adjusted prevalence, Abruzzo vs. south-west London P = 0.008).

Distribution of common risk factors for cardiovascular disease in hypertensive and normotensive individuals

Type of data and unit of measure	Hypertensive women $(n = 131)$	Normotensive women $(n = 671)$	Pª	Hypertensive men $(n=261)$	Normotensive men $(n=541)$	Pª
Age, mean (SE) (years)	49.4 (6.6)	44 (7.7)	< 0.0001	50.3 (7.3)	46.1 (7.3)	< 0.0001
BMI, mean (SE) (kg/m <sup>2</sup> )	29 (5.3)	25.3 (4.5)	< 0.0001	28.7 (4)	26.6 (3.4)	< 0.0001
Waist circumference, mean (SE) (cm)	85.5 (0.5)	85 (0.2)	-	96.6 (0.3)	96 (0.2)	_
WHR, mean (SE)	0.83 (0.005)	0.82 (0.002)	_	0.94 (0.003)	0.93 (0.002)	0.03
Total cholesterol, mean (SE) (mg/dl)	214.6 (3.3)	214.3 (1.4)	-	225.5 (2.5)	221.9 (1.7)	_
LDL cholesterol, mean (SE) (mg/dl)	134.9 (3.1)	138 (1.3)	_	146.8 (2.3)	148 (1.5)	_
HDL cholesterol, mean (SE) (mg/dl)	56.6 (1.2)	57.8 (0.5)	_	49.9 (0.8)	47.4 (0.5)	0.009
Triglycerides, median (Q1-Q3) (mg/dl)	110 (83-153)	76 (60-108)	< 0.0001	129 (91-183)	104 (75-154)	_
Glucose, median (Q1-Q3) (mg/dl)	83 (73-90)	78 (71 – 85)	0.01	85 (76-93)	82 (75-89)	_
Hs-CRP, median (Q1-Q3) (mg/l)	1.67 (0.79-3.38)	1.42 (0.65-2.79)	0.02	1.41 (0.66-3)	1.07 (0.56-2.28)	_
Current smoking-adjusted prevalence (%)	17.2	20.2	_	27.7	26.8	-

HDL, high-density lipoprotein; Hs-CRP, high-sensitivity C reactive protein; LDL, low-density lipoprotein; SE, standard error; WHR, waist-to-hip ratio. a Adjusted for age, BMI, social status and region. (Only BMI, social status and region for comparison of age; only age, social status and region for comparison of BMI).

Table 3 Age, BMI and social status-adjusted prevalence of awareness and treatment in hypertensive patients and control in treated hypertensive patients at the 140/90 mmHg threshold

		Hypertension awareness in hypertensive patients		Hypertension treatment in hypertensive patients		Hypertension control in treated hypertensive patients at 140/ 90 mmHg threshold	
	%	P for sex <sup>a</sup>	%	P for sex <sup>a</sup>	%	P for sex <sup>a</sup>	
South-west London	า					·	
Total <sup>b</sup>	43.4		32.1		47.7		
Women	64.9	0.0003	54.5	0.0009	62.4	_	
Men	29.4		16.6		32.7		
Limburg							
Total <sup>b</sup>	51.6		42.5		43		
Women	58.1	_	52.2	_	57.1	_	
Men	44.4		32.6		28.8		
Abruzzo							
Total <sup>b</sup>	48.1		43.5		42		
Women	49	_	46.2	_	55.6	_	
Men	43.1		36.5		28.3		

<sup>&</sup>lt;sup>a</sup> Age, BMI, social status and region-adjusted prevalence. <sup>b</sup> Age, sex, BMI, social status and region-adjusted prevalence.

Out of those treated for hypertension, only 42, 43 and 47.7% (age, sex, BMI and social status-adjusted prevalence) in Abruzzo, Limburg, south-west London, respectively, reached the target values (Table 3). After exclusion of participants who started antihypertensive therapy in the year of recruitment (10.5%), the percentage of participants on treatment did not change (data not shown).

#### **Discussion**

BP levels, prevalence, awareness, therapy and control of hypertension were evaluated in apparently healthy unrelated male-female pairs from three European communities in the framework of the IMMIDIET project [13].

As shown by several other studies in general populations, both SBP and DBP were higher in men than in women and increased with age. Women from south-west London, although being on average older, had BP levels lower than women from either of the other regions. These results are in apparent contrast with what was expected from the northern-southern European gradient of MI, as defined by the MONICA data [14]; indeed, participants classified at high MI risk (such as the English) had lower levels of BP than those at lower risk (such as the Italians). Italian women also showed a higher prevalence of prehypertension than those from the other two regions, whereas the prevalence of hypertension, measured according to the most recent European guidelines [22], was higher in Italian men, probably because of the lower levels of BP in women than men. Data obtained in larger populations recruited 20 years ago [2,7] showed a higher prevalence of hypertension in English than in Italian people. This apparent discrepancy could be due to a different proportion, in the communities studied, of individuals living alone, with diabetes or cardiovascular disease. All these individuals were excluded from our study and could have a higher level of BP, as suggested by the lower prevalence of hypertension found in all three communities selected for our project. Moreover, it could be partially explained by differences in social level among the communities, as suggested by the decreased difference after adjustment for social status. On the contrary, it could also reflect changes in risk factor prevalence that have occurred during the last two decades [9,11,26]. Recent data from a national survey in England show that SBP and, to a lesser extent, DBP levels progressively declined from 1994 to 2003 [27]. The relatively high prevalence of hypertension (around 29%) measured in the Abruzzo community is in agreement with data reported by more recent studies in Italy using the definition of hypertension according to WHO/International Society of Hypertension guidelines or the Sixth Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure [2,28,29]. Moreover, in a population aged 40-75 years from San Marino Republic (a small independent region in the center of Italy, not far from Abruzzo), hypertension had a prevalence of 46.7%, even higher than the 36% we found in patients from Abruzzo older than 40 years (range of age, 40-64 years) [30].

Our results underline the critical situation of some areas of Italy, especially its southern regions, where more accurate public health campaigns should be launched and more attention to BP and related lifestyles should be paid by physicians and public health officers. Indeed, recent data from the Italian 'Cardiovascular Observatory' (http://www.cuore.iss.it/cuore\_exe/osservatorio.asp) reveal that the incidence of stroke is relatively high in Italy, particularly in some regions including Abruzzo [31].

One of the main focuses of the primary prevention of cardiovascular disease is increasing awareness and treatment of patients with hypertension. This approach has had a positive impact on cardiovascular disease prevention in many countries, especially in the USA where the effort was greatest [7]. However, our study shows that awareness and management of hypertension are far from optimal in all three European areas studied. Our results

are in keeping with data from other European studies [2,7–12] but still remain different from those found in the USA in recent years [32].

No difference was observed in awareness, treatment or control of hypertension among the three populations. Similar to Canada and the USA, men were less aware of being hypertensive and were less likely to receive drug therapy than women [7]. This gap may be related, in part, to the fact that women have more frequent contacts with healthcare practitioners and therefore may benefit better from educational material [33].

On comparing our results with data from recent national surveys [8], the treatment rate in hypertensive patients was similar. Among those pharmacologically treated for hypertension, less than half were controlled, according to the ESH [22]. This may be because of a lack of compliance or concordance with the therapy as well as an underestimation of their condition resulting in a less aggressive treatment. Moreover, clinicians need to overcome clinical inertia and step up maximal efforts to reach the BP target values both with lifestyle and pharmacological treatment. A region-wide survey of more than 5000 general practitioners in a region of north-western Italy showed that only a minority of primary-care physicians had sufficient awareness of current guidelines [29]. Increased patient awareness and compliance together with increased adherence of physicians to current guidelines should help in reducing the long-term cardiovascular consequences of hypertension.

There are some limitations to the present study. We did not define a hypertension status but, similar to most epidemiological surveys [34], measured BP values on one occasion; this procedure has been previously shown to yield false-positive hypertensive cases and a smaller number of false-negative ones. However, the possible overestimation of hypertension should have been offset, at least partly, as BP was measured after 5-min rest by trained research personnel, and the mean values of the last two out of three readings were used for our analyses. In addition, patients had been fasting overnight and had refrained from smoking for at least 6h before BP measurements. All these factors would result in lower BP readings than those obtained in routine clinical practice.

The validity of comparisons between communities depends critically on the comparability of the survey methods. A strength of our study is the careful standardization of clinical procedures and of the scientific personnel in charge and the centralization of all biochemical analyses. Finally, we cannot consider our data as representative of the overall population of Italy, England or Belgium, as they have been obtained in apparently healthy unrelated male–female pairs living in three regions of these countries.

In conclusion, our comparative study of three European communities indicates some variations in the level of BP, especially in women. Furthermore, this study highlights the limited awareness and in appropriate management of hypertension and the urgent need, in different European regions, for an intensive programme to reduce the gap in effective preventive strategies for the control of cardiovascular disease.

# **Acknowledgements**

We are grateful to Professor Jozef Vermylen, Catholic University, Leuven, Belgium, for his critical review of the manuscript.

European Collaborative Group of the IMMIDIET Project.

Project coordinator: Licia Iacoviello<sup>a</sup>; scientific committee: Jef Arnout, <sup>b</sup> Frank Buntinx, <sup>c</sup> Francesco P. Cappuccio, <sup>d</sup> Pieter C. Dagnelie, <sup>e</sup> Maria Benedetta Donati, <sup>a</sup> Michel de Lorgeril, <sup>f</sup> Vittorio Krogh, <sup>g</sup> Alfonso Siani<sup>h</sup>; coordinating secretariat: Carla Dirckx<sup>b,c</sup>; data management and statistics: Augusto Di Castelnuovo<sup>a</sup>; dietary assessment and analysis: Martien van Dongen<sup>e</sup>; communication and dissemination: Americo Bonanni<sup>a</sup>; recruitment: Carla Dirckx, <sup>b,c</sup> Pit Rink, <sup>d</sup> Branislav Vohnout, <sup>a</sup> Francesco Zito<sup>a</sup>.

External advisory committee: Mario Mancini, Napoli, Italy; Antonia Trichopoulou, Athens, Greece

The IMMIDIET group, collaborative centers and associated investigators

- (a) Research Laboratories, Center for High Technology Research and Education in Biomedical Sciences, Catholic University, 86100 Campobasso, Italy (Licia Iacoviello, Francesco Zito, Augusto Di Castelnuovo, Americo Bonanni, Branislav Vohnout, Marco Olivieri, Amalia De Curtis, Agnieszka Pampuch, Maria Benedetta Donati, Giovanni de Gaetano).
- (b) Center for Molecular and Vascular Biology, Katholieke Universiteit Leuven, Leuven, Belgium (Jef Arnout, Carla Dirckx, Ward Achten).
- (c) Department of General Practice, Katholieke Universiteit Leuven, Leuven, Belgium (Frank Buntinx, Carla Dirckx, Jan Heyrman).
- (d) Clinical Sciences Research Institute, Warwick Medical School, Coventry, United Kingdom (Francesco P. Cappuccio, Michelle A Miller); Division of Community Health Sciences, St George's, University of London, United Kingdom (Pit Rink, Sally C Dean, Clare Harper).
- (e) Department of Epidemiology, NUTRIM Subdivision of Nutritional Epidemiology, Maastricht University, Maastricht, The Netherlands (Pieter Dagnelie, Martien van Dongen, Dirk Lemaître).

- (f) Nutrition, Vieillissement et Maladies Cardiovasculaires (NVMCV), UFR de Médecine, Domaine de la Merci, 38056 La Tronche, France (Michel de Lorgeril).
- (g) Nutritional Epidemiology Unit, National Cancer Institute, Milan, Italy (Vittorio Krogh, Sabrina Sieri, Manuela Bellegotti, Daniela Del Sette Cerulli).
- (h) Unit of Epidemiogy and Population Genetics, Institute of Food Sciences CNR, Avellino, Italy (Alfonso Siani, Gianvincenzo Barba, Paola Russo, Antonella Venezia).

The IMMIDIET project was originally supported by European Union grant no. QLK1-2000-00100. MIUR (Ministero dell'Università e Ricerca, Italia), Programma Triennale di Ricerca, grant D. 1588, supported Licia Iacoviello and her associates at the Catholic University in Campobasso, Italy.

# References

- Kearney PM, Whelton M, Reynolds K, Muntner P, Whelton PK, He J. Global burden of hypertension: analysis of worldwide data. Lancet 2005;
- Wolf-Maier K, Cooper RS, Banegas JR, Giampaoli S, Hense H, Joffres M, et al. Hypertension and blood pressure levels in 6 European countries, Canada, and the US. JAMA 2003; 289:2363-2369.
- Baguet JP, Barone-Rochette G, Mallion JM. European Society of Hypertension Scientific Newsletter: hypertension and coronary heart disease. J Hypertens 2006; 24:2323-2325.
- Collins R, McMahon S. Blood pressure, antihypertensive drug treatment and the risks of stroke and of coronary heart disease. Br Med Bull 1994; 50:272-298
- Kannel WB. Blood pressure as a cardiovascular risk factor: prevention and treatment. JAMA 1996; 275:1571-1576.
- Neal B, MacMahon S, Chapman N. Blood Pressure Lowering Treatment Trialists' Collaboration, Effects of ACE inhibitors, calcium antagonists, and other blood-pressure-lowering drugs: results of prospectively designed overviews of randomized trials. Lancet 2000; 356:1955-1964.
- Wolf-Maier K, Cooper RS, Kramer H, Banegas JR, Giampaoli S, Joffres MR, et al. Hypertension treatment and control in five European countries. Canada, and the United States. Hypertension 2004; 43:10-17.
- 8 Erdine S. European Society of Hypertension Scientific Newsletter: update on hypertension management - how well is hypertension controlled in Europe? J Hypertens 2000; 18:1348-1349.
- Patel R, Lawlor DA, Whincup P, Montaner D, Papacosta O, Brindle P, Ebrahim S. The detection, treatment and control of high blood pressure in older British adults: cross-sectional findings from the British Women's Heart and Health Study and the British Regional Heart Study. J Hum Hypertens 2006; 20:733-741.
- Fagard RH, Van den Enden M. Treatment and blood pressure control in isolated systolic hypertension vs diastolic hypertension in primary care. J Hum Hypertens 2003; 17:681-687.
- 11 Fagard RH, Van Den Enden M, Leeman M, Warling X. Survey on treatment of hypertension and implementation of World Health Organization/ International Society of Hypertension risk stratification in primary care in Belgium. J Hypertens 2002; 20:1297-1302.
- Wang YR, Alexander GC, Stafford RS. Outpatient hypertension treatment, treatment intensification, and control in Western Europe and the United States. Arch Intern Med 2007; 167:141-147.
- lacoviello L, Arnout J, Buntinx F, Cappuccio FP, Dagnelie PC, de Lorgeril M, et al. Dietary habit profile in European Communities with different risk of myocardial infarction: the impact of migration as a model of geneenvironment interaction. The IMMIDIET study. Nutr Metab Cardiovasc Dis 2001; 11 (Suppl 4):122-126.
- Tunstall-Pedoe H, Kuulasmaa K, Mahonen M, Tolonen H, Ruokokoski E, Amouyel P. Contribution of trends in survival and coronary-event rates to changes in coronary heart disease mortality: 10-year results from 37 WHO MONICA project populations. Monitoring trends and determinants in cardiovascular disease. Lancet 1999; 353:1547-

- 15 Russo P, Lauria F, Loguercio M, Barba G, Arnout J, Cappuccio FP, et al. -344C/T Variant in the promoter of the aldosterone synthase gene (CYP11B2) is associated with metabolic syndrome in men. Am J Hypertens 2007; 20:218-222.
- 16 Di Castelnuovo S, Quacquaruccio G, Arnout J, Cappuccio FP, de Lorgeril M, Dirckx C, et al. Risk factors and global risk of fatal cardiovascular disease are positively correlated between partners of 802 spouse pairs from different European countries: report from the IMMIDIET project. Thromb Haemost 2007; 98:648-655.
- 17 Dean SC, Harper CE, Cappuccio FP, Rink E, Dirckx C, Arnout J, et al. The challenges of cross-national research in primary health care across Europe. Fam Pract 2005: 22:1-6.
- Cappuccio FP, Strazzullo P, Farinaro E, Trevisan M. Uric acid metabolism and tubular sodium handling: results from a population-based study. JAMA 1993; **270**:354-359.
- O'Brien E, Waeber B, Parati G, Staessen J, Myers MG. Blood pressure measuring devices: recommendations of the European Society of Hypertension. BMJ 2001; 322:531-536.
- 1999 World Health Organization-International Society of Hypertension guidelines for the management of hypertension. Guidelines Subcommittee. J Hypertens 1999: 17:151-183.
- 21 Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults: The Evidence Report. National Institutes of Health Obes Res 1998; 6 (Suppl 2):51S-209S.
- 22 Mancia G, De Backer G, Dominiczak A, Cifkova R, Fagard R, Germano G, et al. 2007 Guidelines for the Management of Arterial Hypertension: The Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). J Hypertens 2007; 25:1105-1187.
- 23 Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr, et al. Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. National Heart, Lung, and Blood Institute; National High Blood Pressure Education Program Coordinating Committee. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Hypertension 2003; 42:1206-1252.
- Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. Clin Chem 1972; 18:499-502.
- SAS Institute Inc. SAS/STAT user guide, version 8.2 for WINDOWS. Cary, North Carolina: SAS Institute Inc; 1989.
- Schuit AJ, Wendel-Vos GC, Verschuren WM, Ronckers ET, Ament A, Van Assema P, et al. Effect of 5-year community intervention Hartslag Limburg on cardiovascular risk factors. Am J Prev Med 2006; 30:237-242
- Primatesta P, Poulter NR. Improvement in hypertension management in England: results from the Health Survey for England 2003. J Hypertens 2006; **24**:1187-1192.
- Menotti A, Lanti M, Zanchetti A, Puddu PE, Cirillo M, Mancini M, Vagnarelli OT. Impact of the Gubbio population study on community control of blood pressure and hypertension. Gubbio Study Research Group. J Hypertens 2001; 19:843-850.
- Cuspidi C, Michev I, Meani S, Severgnini B, Sala C, Salerno M, et al. Lombardy Regional Section of the Italian Society of Hypertension. Awareness of hypertension guidelines in primary care: results of a regionwide survey in Italy. J Hum Hypertens 2003; 17:541-547.
- Mancia G, Parati G, Borghi C, Ghironzi G, Andriani E, Marinelli L, et al. Hypertension prevalence, awareness, control and association with metabolic abnormalities in the San Marino population: the SMOOTH study. J Hypertens 2006; 24:837-843.
- 31 Carolei A, Marini C, Di Napoli M, Di Gianfilippo C, Santalucia P, Baldassarre M, et al. High stroke incidence in the prospective communitybased L'Aquila Registry (1994-1998). First year's results. Stroke 1997; **28**:2500-2506.
- 32 Ong KL, Cheung BM, Man YB, Lau CP, Lam KS. Prevalence, awareness, treatment, and control of hypertension among United States adults 1999-2004. Hypertension 2007; 49:69-75.
- Onysko J, Maxwell C, Eliasziw M, Zhang JX, Johansen H, Campbell NR. Canadian Hypertension Education Program. Large increases in hypertension diagnosis and treatment in Canada after a healthcare professional education program. Hypertension 2006; 48:853-860.
- Volpe M, Tocci G, Trimarco B, Rosei EA, Borghi C, Ambrosioni E, et al. Blood pressure control in Italy: results of recent surveys on hypertension. J Hypertens 2007; 25:1491-1498.