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**DOTTORATO DI RICERCA IN
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TESI DI DOTTORATO

**PREVALENCE OF CARDIOVASCULAR RISK FACTORS
IN A LARGE ITALIAN COHORT**

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Introduction

The concept of risk factors has evolved only over the past 45 years. Since the early 1960s and particularly following the Framingham study in the late 1970s, many factors that predispose to the development of atherosclerosis and cardiovascular disease (CVD) have been thoroughly investigated (1).

The list of these factors, now called cardiovascular risk factors (CRFs), continues to grow and new factors are periodically added to the list as our comprehension of the disease process grows. Extensive clinical and statistical studies have identified several factors that increase the risk of CVD (2, 3, 4, 5).

Major risk factors are those that research has shown significantly increase the risk of heart and blood vessel disease (3).

Some CRFs can't be modified as advanced age, male gender, heredity (including race, family history of CVD), and some can be modified, treated or controlled as smoking, dyslipidemia, hypertension, diabetes

mellitus, physical inactivity, overweight and obesity (especially abdominal obesity). Nowadays other new modifiable CRFs, as alcohol, fruit and vegetables consumption and stress, has been identified. The significance and prevalence of these, called contributing risk factors, have not yet been precisely determined.

Several of these risk factors are interrelated. Obesity, cigarette smoking and lack of exercise adversely influence blood pressure and blood cholesterol levels (6). The greater the level of each risk factor, the greater the risk, and the more risk factors a person has, the greater the likelihood of developing cardiovascular disease (7).

CVD result in substantial disability and loss of productivity and contribute in large part, to the escalating costs of health care, especially in the presence of an ageing population. CVDs are the major cause of death in adults and elderly in the majority of the developed countries and in many developing countries. Papers published by the World Health Organization of the United Nations (WHO) and others (8, 9, 10, 11) have previously reported trends in cardiovascular mortality over time (12).

These reports showed large international between-country differences both in the levels and in the trends in mortality from CVDs with a substantial increase in countries of Central and Eastern Europe concomitant with recent nutritional, economical and political changes (13, 14).

Sans *et al.*(12) reported a clear north–east to south–west gradient in CVD mortality (1990–1992; 45–74 years age-adjusted) with the lowest rates for both men and women in France, Spain, Switzerland, and Italy (12). Regional variations in cardiovascular mortality have been observed both between and within countries in Europe (11, 12, 15, 16). There are many reasons for the observed regional variations. They include differences between populations in “classic” CRFs as well as socio-economic factors and lifestyle variables. These large differences have been also mainly attributed to environmental factors and in particular to differences in dietary pattern, especially in favour of Mediterranean countries where low rates of cardiovascular- and cancer-related mortality have been reported (17). The current European Guidelines on Cardiovascular Disease Prevention in Clinical

Practice take national variation in cardiovascular mortality into account (18).

The improvement of some CRFs seems to be the main reason for the decrease in cardiovascular morbidity and mortality in Italy and in most Western countries over the last decades (19, 20, 21, 22, 23, 24, 25). This is partly due to an early management of CRFs by lifestyle modifications and/or pharmacological intervention with a reduction in their level (26, 27, 28, 29).

An inverse trend can be observed for obesity, whose prevalence is steadily increasing (30, 31, 32, 33). Scientific evidence accumulated over recent years has prompted the American Heart Association to identify obesity as the major and modifiable risk factor for CVDs, and the UK Government (Department of Health) to include obesity as one of the six key priorities in the White Paper *Choosing Health: Making Healthy Choices Easier* and the Italian Ministry of Health to launch the Project '*Guadagnare Salute*' which foresees multidisciplinary interventions in the field of diet and physical activity (2, 34, 35).

In 2005 the French agency for research and information on fresh fruits and vegetables (Aprifel), the Italian Ministry of Health and the National Centre for Disease Prevention and Control (CCM), organized the International Conference on Health Benefits of Mediterranean Style Diet - From Scientific Evidence to Health Prevention Actions - with the aim of highlighting the latest scientific knowledge on health benefits of Mediterranean style diet and the strategic perspectives for health operators (36, 37, 38, 39).

In Italy, latest available data on overweight and obesity come from the multi-scope surveys performed in 2003 and published in 2005, and more recently performed in 2005 and published in 2007 by the Italian Institute of National Statistics (ISTAT), collecting self-reported information on health status (40, 41) and from the Epidemiologic Cardiovascular Observatory (OEC) of the *Progetto CUORE*, estimating prevalence of overweight, obesity and other CVD risk factors in Italian men and women aged 35–74 years examined between 1998 and 2002 (42).

More recently, 2090 Italian men and women aged 35–74 years were screened by general practitioners to assess their cardiovascular risk, lifestyles habits and drug use (43).

Therefore, there is a pressing need to update and collect reliable and comparable data focusing on more recent CRFs to establish a national surveillance and prevention program.

Aim

Aims of this cross-sectional study were to assess the prevalence of CRFs; to describe the alcohol, fruit and vegetables consumption; to investigate the family history of diabetes, hypertension, dyslipidemia and obesity; to evaluate the association between obesity/overweight or high waist circumference and some CRFs, in a large cohort of Italian men and women aged over 18 years, in five Italian macroareas.

Materials and Methods

Screening

The study was performed in 24.609 Italian individuals (men and women), aged over 18 years (mean age of the study population 56.9 ± 15.3 years). The individuals were participants in an information program for the prevention of the metabolic syndrome “*Misuriamoci*”, conducted by the *Croce Rossa Italiana* (CRI) on the 24th and 25th of March 2007 in collaboration with the Italian Association of General Practitioners (SIMG) and “*la Federazione nazionale dei titolari di farmacia italiani*” (*FEDERFARMA*) and supported by the Italian Ministry of Health.

Advertising was conducted by radio and television announcements, spot on ATAC buses and adverts in the pharmacy, supported by Takeda Italia Farmaceutici, Multicare, FederFARMACO and Pacini editore.

The study involved people who spontaneously went to the main squares of 193 Italian cities. A paper questionnaire was developed by Nutrition section of Neuroscience Dpt. of University of Naples “Federico II”. Subjects were asked about their personal data, habits (smoking, physical activity, alcohol consumption, fruit and vegetable consumption), family history of diabetes, hypertension, dyslipidemia and/or obesity, current drug treatments (anti-hypertensive, lipid-lowering, anti-diabetic). Anthropometric (weight, height and waist circumference) and blood pressure measurements were performed using standardized methodologies (standard electronic scale, wall height ruler, tape measure at the level of the umbilicus and mercury sphygmomanometer). Total cholesterol, tryglicerides and blood glucose were assessed in all subjects.

Data analysis

Body mass index (BMI) was calculated as weight (kg) divided by height squared (m^2). The distribution of overweight and obesity was

calculated considering the following categories: overweight as BMI 25.0-29.9 kg/m² and obesity as BMI ≥ 30 kg/m².

Fasting cholesterol, triglycerides and glucose level were collected by finger-prick capillary blood samples using Multicare® diagnostic device (44).

According to the NCEP ATP III criteria (45), abdominal obesity was defined as waist circumference ≥ 102 cm in men and ≥ 88 cm in women. Blood pressure was recorded as the average of two measurements after subjects had been sitting for 5 min. The average of the two readings was used in the analysis. Elevated blood pressure level was considered if having systolic blood pressure ≥ 130 mmHg and/or diastolic blood pressure ≥ 85 mmHg or if they reported taking antihypertensive medication. Hyper-triglyceridemia was considered with serum triglycerides level ≥ 150 mg/dl or if they reported taking anti-dyslipidemic medication (45). Impaired fasting glucose (Hyperglycemia) was defined as a fasting plasma glucose level in the range of 100 mg/dl up to 125.9 mg/dl and diabetes was considered as fasting blood glucose ≥ 126 mg/dl or if they reported taking anti-

diabetic medication (46). High blood total cholesterol was defined as \geq 200 mg/dl or if they reported taking anti-dyslipidemic medication (47). For alcohol intake and fruit and vegetable consumption (fruit&vegetable) a commonly used serving size was specified and subjects were asked “if and how often they had consumed that unit”. Daily and/ or weekly consumption was asked for fruit&vegetable. An average consumption of 3-5 servings-a-day of fruit and vegetables was considered as recommended (48,49, 50,51).

Alcohol intake was recorded as glasses per week (one glass is defined as 4 fl oz of wine). An average daily intake of 1 glass for men and of $\frac{1}{2}$ glass for women was considered as recommended (52).

About the geographic distribution Italy was considered as a whole and the following macroareas (i.e. area comprising more Regions, generally contiguous): Northwest, including data from *Valle d’Aosta, Piemonte, Liguria and Lombardia*; Northeast, including data from *Trentino-Alto Adige, Friuli-Venezia Giulia, Veneto and Emilia Romagna*; Center, including data from *Toscana, Marche, Umbria and Lazio*; South including data from *Campania, Abruzzo, Molise,*

Calabria, Puglia and Basilicata; and Islands including data from *Sicilia and Sardegna*.

Data are expressed as mean \pm SD or frequencies to present continuous or categorical variables. Separate prevalence results are presented for men and women. Qualitative and quantitative variables were compared with parametric and non parametric tests, as appropriate. Logistic regression models were used to estimate the independent relationship between obesity/overweight or high waist circumference and CRF. Potential confounders that were chosen before the analysis included gender, macroarea, fruit&vegetables and alcohol intake. In the multivariate model for obesity/overweigh the high waist circumference was added to the covariates as a confounder and *viceversa*. Analysis were performed using STATA 9.2 SE (Stata Corp., College Station, TX).

Results

The study population aged 18-98 years, is normally distributed as confirmed by the values of the mean (57 ± 15 years) and the median (59 years). The distribution of the examined population among the macroareas and between gender is representative of the Italian population (53).

The main demographic, clinical and metabolic characteristics of the study population according to gender and macroarea are shown in table 1. The mean BMI is 26.9 ± 4.4 with men showing a higher mean than women (27.5 ± 3.9 vs 26.2 ± 4.9). Mean waist circumference value of women exceeded the gender-specific cut-off (women: 91 ± 13 ; men: 101 ± 11). The average of systolic blood pressure value is high (134 ± 19) and men are affected more than women (136 ± 18 vs 132 ± 19). Plasma triglycerides mean level also is high (153 ± 81) and women show higher levels than men (158 ± 84 vs 149 ± 78).

Table 2 shows the prevalence of some CRFs in the study population according to gender and macroarea. 22% of the population is identified as obese and 41% as overweight. The prevalence of obesity and overweight is different in each macroarea. In particular, the highest prevalence of obesity (27%) is shown by South population, while the lowest one (16%) is shown by North-east population; moreover, the highest prevalence of overweight (44%) is shown by Islands population, while the lowest one (40%) is shown by North-west population. Men are affected more than women both in the study population and in each macroarea.

According to waist circumference cut off, the prevalence of abdominal obesity is 56% in the study population; South population shows the highest prevalence (59%), while North-east population shows the lowest one (52%). Women are affected more than men.

In the study population the prevalence of smoking is 19%; Islands population shows the highest prevalence (24%), while North-west population shows the lowest one (15%). Men smoke more than women.

The total prevalence of hypertension is 73%; both North-west and North-east population show the highest prevalence (76%), while Islands population shows the lowest one (67%). Men are affected more than women.

In the study population the prevalence of hypertriglyceridemia and hypercholesterolemia is 42% and 36% respectively. A higher prevalence of hypertriglyceridemia and hypercholesterolemia is observed in North-west, North-east and Center population compared to South and Islands ones. Women are affected more than men.

The prevalence of diabetes mellitus is 15% in all subjects; South and Islands population show a higher prevalence than North-west, North-east and Center population. Men are affected more than women.

The total prevalence of hyperglycemia is 13%, and the highest prevalence is shown by Center population (18%). Men are affected more than women.

By comparing the dietary pattern with the nutritional guidelines established by the major scientific associations (48, 49, 50) in order to prevent the major chronic diseases, we have found that the study

population reports an alcohol consumption higher than the recommended range in the 23% of the study population with a similar prevalence between gender. In particular, North-west and North-east population show an almost doubled prevalence of people reporting an alcohol consumption higher than the recommended range compared to South and Islands population (Table 3).

66% of the study population shows a fruit and vegetables consumption in the recommended range. Women adhere more than men to the nutritional norm for fruit&vegetable. Geographic distribution show that in North-west, North-east and Center population the prevalence of people showing a fruit and vegetable consumption in the recommended range is higher than South and Islands population (Table 3).

According to family history of CRF 45% of the study population shows a family history of hypertension, 33% of diabetes, 26% dyslipidemia while only 17% shows a family history of obesity (Table 4). Women show a higher prevalence of family history of CRFs than men. North-west population show the highest prevalence of family

history of hypertension, obesity and dyslipidemia, while the highest prevalence of family history of diabetes is found in Islands population.

As overweight and obesity have reached epidemic proportions worldwide (54), and the metabolic consequences of obesity are well documented (55, 56, 57), we have examined the association between overweight/obesity and CRFs adjusted for high waist circumference, gender, macroarea, fruit&vegetable and alcohol intake. Diabetes, hypertriglyceridemia and hypertension are positively associated with overweight/obesity while a negative association is found between overweight/obesity and age, smoking and hypercholesterolemia (Table 5).

Table 6 shows the association with high waist circumference of CRFs adjusted for overweight/obesity, gender, macroarea, fruit&vegetable and alcohol intake. Age, diabetes, hypertension, hypertriglyceridemia show a positive association with high waist circumference. No association is found between high waist circumference and hypercholesterolemia and smoking.

Figure 1 shows the distribution of subjects having one or more CRFs in the study population. The prevalence of subjects with three or four CRFs is quite high (19.6% and 20.7%, respectively) and the prevalence of subjects having between two and five CRFs is 72.0 %.

Discussion

This study provides information about the prevalence and distribution of some CRFs in a representative adult Italian population, which includes 24.609 subjects aged 18-98 years.

The incidence of obesity has increased dramatically in the last years and have become an epidemiological emergency (32, 42, 58). This is confirmed by our results that show a mean value of BMI ($26.9 \text{ Kg/m}^2 \pm 4.4$) falling in the overweight category for both men (27.5 ± 3.9) and women (26.2 ± 4.9). By comparing our results with data from the ISTAT survey (41), the prevalence of obesity has considerably increased over the last few years (22% vs 9.8%) while the prevalence of overweight has only slightly increased (41% vs 34.2%). A possible explanation for the discrepancy in obesity prevalence, may be due to the self-report data used by ISTAT compared to the direct measurements used in our study. Studies based on self-reported and direct measurements show different results in the obesity

prevalence; in fact, obese subjects tend to overestimate their high and to underestimate their weight, leading to an underestimation of the obesity prevalence (59). On the other hand, comparing our data with previous studies (42, 43, 60) using direct measurements, almost the same prevalences of obesity and overweight are found. The prevalence of obesity is quite similar between men and women, while the prevalence of overweight is quite doubled in men than women according to previous reports (41, 43) (Table 2). A possible explanation could be that women, nowadays, pay great attention to weight control. According to ISTAT (41), South population shows the highest prevalence of obesity while a lower prevalence of overweight is found in the North-west population.

By comparing our results with data from the Epidemiologic Cardiovascular Observatory (OEC) of the *Progetto CUORE* (42), we found an increase in the mean waist circumference value both in men (101cm vs 95cm) and women (91cm vs 85cm), and the prevalence of abdominal obesity, as exceeding gender specific waist circumference cut-off, is higher in women than in men (62% vs 51%) (43, 61) and in

South (59%) than in other macroareas. This agrees with a positive trend of the waist circumference gradient observed over the last few years (62).

Obesity and waist circumference result in various metabolic disorders that raise the risk of CVDs (63, 64). High triglyceride level has been observed in subjects with abdominal obesity (65), and hypertriglyceridemia is a well-known risk factor of CVDs (66, 67). Interestingly in our study the prevalence of hyper-triglyceridemia is almost doubled than in previous study (42). This could be the result of unhealthy eating habits and increased intake of fast foods and other high fat content food, in the Italian population over the last years.

In the same way, the prevalence of diabetes and hyperglycemia are almost doubled compared to previous surveys (41, 42); while the prevalence of diabetes is similar when compared to a more recent study (43). These findings are important as they represent an alarming risk for CVDs.

On the contrary, in our study the prevalence of hypercholesterolemia is lower than in previous survey (42), although it is similar when

compared with a more recent study (43). Therefore, over the last few years it seems to exist a positive trend in the prevalence of some metabolic parameters as hypertriglyceridemia, diabetes and hyperglycemia, and a negative trend in the prevalence of hypercholesterolemia. In addition, according to previous studies (42, 61, 68), men show a higher prevalence of diabetes (17 % vs 12%) and hyperglycemia (14% vs 12%) than women; while women show a higher prevalence of hypercholesterolemia (42% vs 30%) and hypertriglyceridemia (45% vs 40%) than men (69).

However, the most important finding is that hypertension is the main CRF in the study population (73%). Our data show a prevalence of hypertensive people much higher than ISTAT (12.9%; 13.6%) (40,41) and OEC (48.5%) (42) data. Possible explanations of this finding are that ISTAT survey considered a wide age range (0 – over 80 years), and used self-reported data that underestimate the prevalence of hypertension because it does not include people not aware of being suffering from hypertension. Moreover, according to more recent guide-lines (45) we used cut-off point for hypertension lower than

those used in previous studies (40, 41, 42). According to gender, men are affected by hypertension more than women (42,43). The distribution of hypertension prevalence in the five examined macroareas is different comparing our study with previous ones (40, 42), except for the lowest prevalence in Islands (40) and the highest prevalence in North-east (42).

The trend of smoking prevalence seems to be reduced comparing our data (19%) with both OEC (25.5%) and ISTAT ones (23.9%; 21.7%), even if in these studies the age of the examined populations are not strictly overlapped (40, 41, 42). Differences could also be ascribed to the different period of screening; in fact, the trend of people who quit smoking has increased over the last few years (41) and this could be maybe due to huge national prevention programs and also to the introduction of the Italian anti-smoking legislation in January 2005, banning smoking in public places. Moreover, according to previous studies men smoke more than women (40, 41, 42), with an almost doubled prevalence in South macroarea; and South and Islands show the highest prevalence of smokers (42).

Over the last 50 years, many studies have evaluated the associations between food groups and chronic diseases, and a consensus about the role of nutritional factors in the aetiology of these diseases has gradually emerged (70, 71, 72). In particular, data from epidemiological studies showed that increased consumption of fruit and vegetables can reduce the overall mortality in both healthy subjects and patients (73). Actually, nutritional recommendations for fruit&vegetables have been recently reviewed and have been raised from the five servings-a-day to the more ambitious seven (or nine) servings-a-day (51). Unfortunately, the average daily intake of fruit and vegetables has not simultaneously increased over the last years. In fact, even by considering the recommended range between 3 and 5 servings-a-day according to the major scientific associations (48, 49, 50, 51), only 66% of the study population reach the optimal intake for fruit and vegetables, and many subjects are far from reaching the optimal intake for these foods (69). It is interesting that in North-west, North-east and Center population the prevalence of people showing a fruit and vegetable consumption in the recommended range is higher

than South and Islands population. A possible explanation for this finding could be related to a low household income (74).

No recent surveys have examined wine intake according to the range that we consider as recommended in our study (52). The prevalence of people who has declared a wine intake in the recommended range (77%) could be considered acceptable. According to ISTAT (40), the prevalence of people showing a higher alcohol consumption than recommended is almost doubled in North-west, North-east and Center population compared to South and Islands population.

As the risk factors are individually important, having more than one risk factor tend to magnify the risk of chronic disease (75).

Our study shows that 89 % of the study population has more than one CRF for CVD and we think that these results are alarming. Moreover, as hypertension (73%), obesity/overweigh (63%), diabetes (15%) and dyslipidaemia (hypertriglyceridemia 42% and hypercholesterolemia 36%) occur frequently in the study population, it is not surprising that an individual might manifest two or more of these disorders. In agreement with data from a study of Caucasian populations (76) our

study finds an overlapping pattern of CRFs in the Italian population, and much more than half of the study population has between two and five risk factors (72%), with 17% of the examined population having six or more risk factors (figure 1).

Since in our study obesity/overweight and high waist circumference are both independently associated with the same CVRFs (hypertension, hypertriglyceridemia and diabetes) in a multiple logistic regression model (Table 5 and 6), both obesity/overweight and high waist circumference represent a serious health concern. Therefore it should be very important to inform people about the possible association between obesity *per se* and/or high waist circumference and other CRFs. Moreover, BMI and waist circumference may be a good choice in clinical practice and could be useful to alert people.

Interestingly, the highest prevalence of family history of both hypertension (53%) and dislipidemia (30%) is found in North-west population according to the highest prevalence of hypertension (76%) and hypercholesterolemia (39%) in this macroarea. In addition, the lowest prevalence of both obesity (16%) and diabetes (12%) such as of

family history of both obesity (16%) and diabetes (30%) are found in North-east, and the lowest prevalence hypertension (67%) and of family history of hypertension (42%) is shown by Islands population. Moreover, the highest prevalence of a positive family history of all the examined CRFs is found in women; this could be maybe explained by the cultural habits and psychological inclination of women taking more care of parents' health than men.

In conclusion, the strength of our study is that we have analyzed several, classical and new, CRFs in a large sample of the Italian population using direct measurements. Our data reveal alarming results on the prevalence of some CRFs, highlighting the need of several approaches to identify individuals at risk by using simple anthropometric parameters and clinical markers as screening tools. Moreover, our findings also emphasize the importance to plan early and urgent appropriate intervention programs aimed at modifying lifestyle and eating habits in the Italian population and aimed at preventing CVDs. In particular it could be very important to plan

intervention programs taking into account the differences among macroareas in the prevalence of CRFs.

References

- 1) Gordon T, Castelli WP, Hjortland MC, Kannel WB, Dawber TR - Predicting coronary heart disease in middle-aged and older persons. The Framington study. *JAMA* 1977; 238: 497–499
- 2) Eckel RH, Krauss RM- American Heart Association call to action: obesity as a major risk factor for coronary heart disease. AHA Nutrition Committee. *Circulation* 1998; 97: 2099-2100
- 3) Stamler J, Stamler R, Neaton JD, Wentworth D, Daviglius ML, Garside D, Dyer AR, Liu K, Greenland P- Low risk-factor profile and long-term cardiovascular and noncardiovascular mortality and life expectancy: findings for 5 large cohorts of young adult and middle-aged men and women. *JAMA* 1999; 282: 2012-2018
- 4) Rosengren A, Dotevall A, Eriksson H, Wilhelmsen L- Optimal risk factors in the population: prognosis, prevalence, and secular trends. Data from Göteborg population studies. *Eur Heart J* 2001; 22: 136-144

- 5) Stampfer MJ , Hu FB, Manson JE, Rimm EB, Willett WC- Primary prevention of coronary heart disease in women through diet and lifestyle. *N Engl J Med* 2000; 343: 16–22
- 6) Benetou V, Bamia C, Trichopoulos D, Mountokalakis T, Psaltopoulou T, Trichopoulou A- The association of body mass index and waist circumference with blood pressure depends on age and gender: a study of 10,928 non-smoking adults in the Greek EPIC cohort. *Eur J Epidemiol*. 2004; 19: 803-809
- 7) Trevisan M, Liu J, Bahsas F, Menotti A, The Risk Factor and Life Expectancy Research Group- Syndrome X and mortality: a population-based study. *Am J Epidemiol* 1998; 148: 958-966
- 8) Pisa Z, Uemura K- Trends of mortality from ischaemic heart % disease and other cardiovascular diseases in 27 countries 1968-1977. *World Health Stat Q* 1982; 35: 11-47
- 9) Uemura K, Pisa Z- Trends in cardiovascular disease mortality industrialized countries since 1950. *World Health Stat Q* 1988; 41: 155-178

- 10) Thom TJ- International mortality from heart disease: rates and trends. *Int J Epidemiol* 1989; 18: S20-8
- 11) Thom TJ, Epstein FH, Feldman JJ, Leaverton PE- Trend in total mortality and mortality from heart disease in 26 countries from 1950 to 1978. *Int J Epidemiol* 1985; 14: 510-520
- 12) Sans S, Kesteloot H, Kromhout D- The burden of cardiovascular diseases mortality in Europe. Task Force of the European Society of Cardiology on Cardiovascular Mortality and Morbidity Statistics in Europe. *Eur Heart J* 1997; 18: 1231–1248
- 13) Kesteloot H- Nutrition and health. *Eur Heart J* 1992; 13: 120-128
- 14) Bobak M, Marmot M- East-West mortality divide and its potential explanations: proposed research agenda. *BMJ* 1996; 312: 421-425
- 15) Müller-Nordhorn J, Rossnagel K, Mey W, Willich SN- Regional variation and time trends in mortality from ischaemic heart disease: East and West Germany 10 years after reunification. *J Epidemiol Community Health* 2004; 58: 481-485

16) Health statistics. Atlas on mortality in the European Union. Data 1994–97. (2002) Luxembourg: Office for Official Publications of the European Communities

17) Keys A, Menotti A, Karvonen MJ, Aravanis C, Blackburn, Buzina R, Djordjevic BS, Dontas AS, Fidanza F, Keys MH, Kromhout D, Nedeljkovic S, Punsar S, Seccareccia F, Toshima H.- The diet and 15-year death rate in the seven countries study. *Am J Epidemiol* 1986; 124: 903-915

18) De Backer G, Ambrosioni E, Borch-Johnson K, Brotons C, Cifkova R, Dallongeville J, Ebrahim S, Faergeman O, Graham I, Mancia G, Manger Cats V, Orth-Gomér K, Perk J, Pyörälä K, Rodicio JL, Sans S, Sansoy V, Sechtem U, Silber S, Thomson T, Wood D- European guidelines on cardiovascular disease prevention in clinical practice. Third Joint Task Force of European and Other Societies on Cardiovascular Disease Prevention in Clinical Practice. *Eur Heart J* 2003; 24: 1601–1610

- 19) Nicolosi A, Casati S, Taioli E, Polli E- Death from cardiovascular disease in Italy, 1972–1981: decline in mortality rates and possible causes. *Int J Epidemiol* 1988; 17: 766-772
- 20) Massarelli G, Muscari A, Hanau C, Paradossi U, Puddu P- Mortality rates and number of deaths from cardiovascular diseases in Italy from 1982 to 1993. A comparison with total and tumor data. *Int J Cardiol* 2000; 75: 37–42
- 21) Menotti A- Cardiovascular risk factors in Italy. *Prev Med* 1999; 29: S111–S118
- 22) Menotti A, Scanga M- Trends in coronary risk factors in Italy. The Responsible Investigators of the RF2, Ob43 and MICOL Research Groups. *Int J Epidemiol* 1992; 21: 883–892
- 23) Menotti A, Seccareccia F, Lanti M, The RIFLE Research Group- Mean levels and distribution of risk factors in Italy in the 1970s and the 1980s. The Italian RIFLE Pooling Project. Risk factors and life expectancy. *G Ital Cardiol* 1995; 25: 1539–1572

- 24) Kesteloot H, Sans S, Kromhout D- Evolution of all-causes and cardiovascular mortality in the age-group 75–84 years in Europe during the period 1970–1996; a comparison with worldwide changes. *European Heart Journal* 2002; 23: 384-398
- 25) Kesteloot H, Sans S, Kromhout D- Dynamics of cardiovascular and all-cause mortality in Western and Eastern Europe between 1970 and 2000. *Eur Heart J* 2006; 27: 107-113
- 26) UK Prospective Study of Therapies of Maturity-Onset Diabetes, I, Effect of diet, sulphonylurea, insulin or biguanide therapy on fasting plasma glucose and body weight over one year. *Diabetologia* 1983; 24: 404–411
- 27) Goldstein DJ- Beneficial health effects of a modest weight loss. *Int J Obes* 1992; 16: 397-415
- 28) WHO, Obesity: Preventing and Managing the Global Epidemic, World Health Organization, Geneva, Switzerland, 2000
- 29) Panico S, Palmieri L, Donfrancesco C, Vanuzzo D, Chiodini P, Cesana G, Ferrario M, Mattiello A, Pilotto L, Segà R, Giampaoli S, Stamler J- Preventive potential of body mass reduction to lower

cardiovascular risk: the Italian Progetto CUORE study. *Prev Med* 2008; 47: 53-60

30) Poirier P, Giles TD, Bray GA, Hong Y, Stern JS, Pi-Sunyer FX, Eckel RH- Obesity and cardiovascular disease: pathophysiology, evaluation, and effect of weight loss. *Arterioscler Thromb Vasc Biol* 2006; 26: 968-976

31) Beer-Borst S, Morabia A, Hercberg S, Vitek O, Bernstein MS, Galan P, Galasso R, Giampaoli S, Houterman S, McCrum E, Panico S, Pannozzo F, Preziosi P, Ribas L, Serra-Majem L, Verschuren WM, Yarnell J, Northridge ME S- Obesity and other health determinants across Europe: the EURALIM project. *J Epidemiol Community Health* 2000; 54: 424-430

32) Haftenberger M, Lahmann PH, Panico S, Gonzalez CA, Seidell JC, Boeing H, Giurdanella MC, Krogh V, Bueno-de-Mesquita HB, Peeters PH, Skeie G, Hjartaker A, Rodriguez M, Quirós JR, Berglund G, Janlert U, Khaw KT, Spencer EA, Overvad K, Tjønneland A, Clavel-Chapelon F, Tehard B, Miller AB, Klipstein-Grobusch K, Benetou V, Kiriazi G, Riboli E, Slimani N- Overweight, obesity and

fat distribution in 50- to 64-year-old participants in the European Prospective Investigation into Cancer and Nutrition (EPIC). *Public Health Nutr* 2002; 5: 1147-1162

33) Atlante italiano delle malattie cardiovascolari, II Edizione, Osservatorio Epidemiologico Cardiovascolare italiano. *Ital. Heart J* 2004; 5: 49S–93S

34) Department of Health- Choosing Health: Making Healthier Choices Easier. *Cm 6374*. The Stationery Office: London, 2004

35) Italian Ministry of Health
[<http://www.ministerosalute.it/stiliVita/stiliVita.jsp>] *website*

36) Esposito K, Marfella R, Ciotola M, Di Palo C, Giugliano F, Giugliano G, D'Armiento M, D'Andrea F, Giugliano G- Effect of a mediterranean-style diet on endothelial dysfunction and markers of vascular inflammation in the metabolic syndrome: a randomized trial. *JAMA* 2004; 292: 1440-1446

37) Knoops KT, de Groot LC, Kromhout D, Perrin AE, Moreiras-Varela O, Menotti A, van Staveren WA- Mediterranean diet, lifestyle

factors, and 10-year mortality in elderly European men and women: the HALE project. *JAMA* 2004; 292: 1433-1439

38) Sofi F, Vecchio S, Giuliani G, Marcucci R, Gori AM, Fedi S, Casini A, Surrenti C, Abbate R, Gensini GF- Dietary habits, lifestyle and cardiovascular risk factors in a clinically healthy Italian population: the 'Florence' diet is not Mediterranean. *European Journal of Clinical Nutrition* 2005; 59, 584-591

39) 32 International Conference on Health Benefits of Mediterranean Style Diet. [http://www.aprifel.com/_pdf/MinutesEGEA_2005_1.pdf]

40) ISTAT 2005 : Stili di vita e condizioni di salute, Indagine multiscopo sulle famiglie “Aspetti della vita quotidiana”, 2003. [http://www.istat.it/dati/catalogo/20051118_00/]

41) ISTAT 2007: Condizioni di salute, fattori di rischio e ricorso ai servizi sanitari. [http://www.istat.it/salastampa/comunicati/non_calendario/20070302_00/]

42) Osservatorio Epidemiologico Cardiovascolare Italiano. *Ital Heart J* 2004, 5: 49S-92S

43) Donfrancesco C, Lo Noce C, Brignoli O, Riccardi G, Ciccarelli P, Dima F, Palmieri L, Giampaoli S- Italian network for obesity and cardiovascular disease surveillance: A pilot project. *BMC Fam Pract* 2008; 9: 53

44) [<http://www.multicare.it>]

45) Grundy SM, Cleeman JJ, Daniels SR, Donato KA, Eckel RH, Franklin BA, Gordon DJ, Krauss RM, Savage PJ, Smith SC Jr, Spertus JA, Costa F; American Heart Association; National Heart, Lung, and Blood Institute- Diagnosis and management of the metabolic syndrome. An American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement. *Circulation* 2005; 112: 2735-2752

46) American Diabetes Association Standards of medical care in diabetes—2007. *Diabetes Care* 2007; 30: S4-S41

47) National Heart, Lung and Blood Institute (2007). High blood cholesterol: what you need to know. [<http://www.nhlbi.nih.gov/health/public/heart/chol/wyntk.htm>]

- 48) World Health Organization Study Group- Diet, nutrition, and the prevention of chronic diseases. Technical report series, 916, World Health Organization, Geneva, Switzerland (2003)
- 49) Linee Guida per una Sana Alimentazione Italiana. Revisione 2003. Istituto Nazionale di Ricerca per gli Alimenti e la Nutrizione (INRAN). [<http://www.inran.it>]
- 50) Livelli di Assunzione Giornalieri Raccomandati di Nutrienti per la Popolazione Italiana (L.A.R.N.). Società Italiana di Nutrizione Umana, Revisione 1996. [<http://www.sinu.it/larn>]
- 51) Joint FAO/WHO Workshop on Fruit and Vegetables for Health (2004 : Kobe, Japan)
- 52) “Elaborazione del tipo di dieta verso cui indirizzare il cittadino, consigliando le opportune variazioni” Piano Sanitario Nazionale 2003/2005, approvato con DPR 23 maggio 2003. [http://www.latteriadipiadena.it/files/news/attachments/CIRCOLARE_83_allegato.doc]
- 53) Bilancio demografico nazionale (2007). [<http://demo.istat.it>]

- 54) Wickelgren I- Obesity: how big a problem?. *Science* 1998; 280: 1364-1367
- 55) Hu FB, Manson JE, Stampfer MJ, Colditz G, Liu S, Solomon CG, Willett WC.- Diet, lifestyle, and the risk of type 2 diabetes mellitus in women. *N Engl J Med* 2001; 345: 790-797
- 56) Felber JP, Golay A, Jéquier E, Curchod B, Temler E, DeFronzo RA, Ferrannini E. - The metabolic consequences of long-term human obesity. *Int J Obes* 1988; 12: 377-389
- 57) Keith N- Symposium on ‘Obesity and metabolic diseases’ Obesity and metabolic disease: is adipose tissue the culprit?. *Fraysn Proceedings of the Nutrition Society* (2005), 64, 7–13
- 58) Beer-Borst S, Morabia A, Hercberg S, Vitek O, Bernstein MS, Galan P, Galasso R, Giampaoli S, Houterman S, McCrum E, Panico S, Pannozzo F, Preziosi P, Ribas L, Serra-Majem L, Verschuren WM, Yarnell J, Northridge ME- Obesity and other health determinants across Europe: the EURALIM project. *J Epidemiol Community Health* 2000; 54: 424-430

- 59) Kuskowska-Wolk A, Karlsson P, Stolt M, Rössner S- The predictive validity of body mass index based on self-reported weight and height. *Int J Obes*. 1989; 13: 441-453
- 60) Berghöfer A, Pischon T, Reinhold T, Apovian CM, Sharma AM, Willich SN- Obesity prevalence from a European perspective: a systematic review. *BMC Public Health* 2008; 8: 20
- 61) Miccoli R, Bianchi C, Odoguardi L, Penno G, Caricato F, Giovannitti MG, Pucci L, Del Prato S- Prevalence of the metabolic syndrome among Italian adults according to ATP III definition. *Nutr Metab Cardiovasc Dis* 2005; 15: 250-254
- 62) Ike SO, Chandra DKM, Boev A, Boltri JM, Choi ST, Parish DC, Dever AGE- Abdominal adiposity in U.S. adults: prevalence and trends, 1960–2000. *Preventive Medicine* 2004; 39: 197-206
- 63) St-Pierre J, Lemieux I, Vohl MC, Perron P, Tremblay G, Despres JP, Gaudet D- Contribution of abdominal obesity and hypertriglyceridemia to impaired fasting glucose and coronary artery disease. *Am J Cardiol* 2002; 90: 15–18

- 64) Pi-Sunyer FX- The obesity epidemic: pathophysiology and consequences of obesity. *Obes Res* 2002; 10: 97S–104S
- 65) Bard JM, Charles MA, Juhan-Vague I, Vague P, André P, Safar M, Fruchart JC, Eschwege E; BIGPRO Study Group- Accumulation of triglyceride-rich lipoprotein in subjects with abdominal obesity: the biguanides and the prevention of the risk of obesity (BIGPRO) 1 study. *Arterioscler Thromb Vasc Biol.* 2001; 21: 407-414
- 66) Coughlan BJ, Sorrentino MJ- Does hypertriglyceridemia increase risk for CAD? Growing evidence suggests it plays a role. *Postgrad Med* 2000; 108: 77–84
- 67) Voors AA, van Brussel BL, Kelder JC, Plokker HW- Usefulness of hypertriglyceridemia in predicting myocardial infarction late after coronary artery bypass operation. *Am J Cardiol* 1997; 79: 1350-1354
- 68) Verhave JC, Hillege HL, Burgerhof JG, Navis G, de Zeeuw D, de Jong PE; PREVEND Study Group- Cardiovascular Risk Factors Are Differently Associated with Urinary Albumin Excretion in Men and Women. *J Am Soc Nephrol* 2003; 14: 1330-1335

- 69) Sofi F, Innocenti G, Dini C, Masi L, Battistini NC, Brandi ML, Rotella CM, Gensini GF, Abbate R, Surrenti C, Casini A- Low adherence of a clinically healthy Italian population to nutritional recommendations for primary prevention of chronic diseases. *Nutr Metab Cardiovasc Dis* 2006; 16: 436-444
- 70) Keys A, Menotti A, Karvonen MJ, Aravanis C, Blackburn H, Buzina R, et al. - The diet and 15-year death rate in the seven countries study. *Am J Epidemiol* 1986; 124: 903-915
- 71) Hu FB, Rimm EB, Stampfer MJ, Ascherio A, Spiegelman D, Willett WC- Prospective study of major dietary patterns and risk of coronary heart disease in men. *Am J Clin Nutr* 2000; 72: 912-921
- 72) Farchi G, Fidanza F, Grossi P, Lancia A, Mariotti S, Menotti A- Relationship between eating patterns meeting recommendations and subsequent mortality in 20 years. *Eur J Clin Nutr* 1995; 49: 408-419
- 73) Trichopoulou A, Costacou T, Bamia C, Trichopoulos D- Adherence to a Mediterranean diet and survival in a Greek population. *N Engl J Med* 2003; 348: 2599-2608

- 74) Giskes K, Turrell G, Patterson C, Newman B- Socio-economic differences in fruit and vegetable consumption among Australian adolescents and adults. *Public Health Nutr* 2002; 5: 663-669
- 75) Poulter N- Coronary heart disease is a multifactorial disease. *Am J Hypertens* 1999; 12: 92S-95S
- 76) Modan M, Halkin H, Almog S, Lusky A, Eshkol A, Shefi M, Shitrit A, Fuchs Z. - Hyperinsulinemia: a link between hypertension, obesity and glucose intolerance. *J Clin Invest* 1985; 75: 809-817
- 77) Chan JM, Rimm EB, Colditz GA, Stampfer MJ, Willett WC- Obesity, fat distribution, and weight gain as risk factors for clinical diabetes in men. *Diabetes Care* 1994; 17: 961-969

Table 1. Main demographic, clinical and metabolic characteristics of the study population by gender and macroarea

	Study population			North-west			North-east			Center			South			Islands		
	M	F	Tot	M	F	Tot	M	F	Tot	M	F	Tot	M	F	Tot	M	F	Tot
n.	12626	11587	24609	1585	1892	3477	1692	2101	3793	3032	3114	6146	4650	3438	8088	1667	1042	2709
Age (years)	58±15	55±15	57±15	59±14	58±14	58±14	58±15	57±15	58±15	59±15	56±15	57±15	58±15	53±16	56±16	57±15	52±16	55±16
Weight (Kg)	80±12	66±12	73±14	80±12	65±12	72±14	81±12	66±12	73±14	80±12	66±12	73±14	79±13	68±13	74±14	78±12	65±11	73±13
BMI (Kg/m ²)	27.5±3.9	26.2±4.9	26.9±4.4	27.0±3.9	25.5±4.7	26.2±4.4	26.8±3.7	25.3±4.3	26.0±4.1	27.3±3.7	26.1±4.7	26.7±4.3	28.0±3.9	27.1±5.1	27.6±4.5	27.5±3.8	26.0±4.6	26.9±4.2
Waist Circumference (cm)	101±11	91±13	97±13	100±11	90±13	95±13	100±11	90±12	95±13	100±10	91±13	96±12	103±12	94±15	99±14	102±12	89±13	97±14
Systolic blood pressure (mmHg)	136±18	132±19	134±19	139±18	135±20	137±19	139±19	134±19	136±19	137±18	132±19	135±19	136±18	131±20	134±19	131±16	126±17	129±16
Diastolic blood pressure (mmHg)	81±11	79±11	80±11	82±10	80±10	81±10	81±11	80±11	80±11	81±11	79±11	80±11	81±11	79±11	80±11	79±10	77±10	78±10
Total Cholesterol (mg/dl)	182±33	190±35	186±34	184±29	192±32	188±31	181±34	190±35	186±35	182±36	191±37	187±36	183±32	189±34	185±33	180±31	190±39	184±34
Triglycerides (mg/dl)	149±78	158±84	153±81	144±75	164±85	155±81	159±86	169±90	164±88	150±78	162±86	156±83	150±77	150±79	150±78	143±71	146±74	144±72
Blood Glucose (mg/dl)	86±37	81±30	83±34	87±35	80±27	83±31	83±29	79±25	81±27	88±33	85±31	87±32	79±33	84±39	82±37	78±31	86±43	83±39

Data are expressed as n. or mean ± SD as appropriate

Table 2. Prevalence of some cardiovascular risk factors in the study population by gender and macroarea

	Study population			North-west			North-east			Center			South			Islands		
	M	F	Tot	M	F	Tot	M	F	Tot	M	F	Tot	M	F	Tot	M	F	Tot
Obesity %	23	20	22	19	17	18	17	14	16	21	19	20	28	26	27	23	19	21
Overweight %	51	34	41	50	32	40	51	36	43	52	35	43	48	36	43	51	34	44
High Waist Circumference %	51	62	56	48	58	53	47	57	52	48	64	55	54	67	59	55	59	56
Smoking %	22	15	19	17	13	15	18	15	17	21	18	19	25	13	20	27	20	24
Hypertension %	78	67	74	82	71	76	81	72	76	79	66	73	78	65	72	72	59	67
Hypertriglyceridemia %	40	45	42	38	49	44	43	47	45	42	48	45	39	40	40	36	38	37
Hypercholesterolemia %	30	42	36	32	45	39	31	44	38	31	42	37	30	39	34	29	42	34
Diabetes %	17	12	15	16	13	14	14	11	12	15	11	13	19	14	17	18	12	16
Hyperglycemia %	14	12	13	15	12	13	13	9	11	19	17	18	11	10	10	11	8	10

Table 3. Prevalence of fruits&vegetables and alcohol consumption in the study population by gender and macroarea

	Study population			North-west			North-east			Center			South			Islands		
	M	F	Tot	M	F	Tot	M	F	Tot	M	F	Tot	M	F	Tot	M	F	Tot
Fruit&Vegetables [°] (%)	63	70	66	72	77	75	74	81	78	68	75	72	55	56	56	57	65	60
Alcohol* (%)	23	23	23	32	29	30	28	28	28	25	25	25	20	17	18	16	16	16

[°] Fruits&Vegetables consumption between the recommended range (3 - 5 servings/day)

* Alcohol considered as wine consumption higher than recommended intake (>1 glass for men, >½ glass for women)

Table 4. Family history of some cardiovascular risk factors in the study population by gender and macroarea

	Study population			North-west			North-east			Center			South			Islands		
	M	F	Tot	M	F	Tot	M	F	Tot	M	F	Tot	M	F	Tot	M	F	Tot
Family history of Obesity (%)	15	21	17	16	22	19	14	18	16	15	21	18	16	21	18	14	20	16
Family history of Hypertension (%)	38	54	45	44	60	53	35	48	42	41	54	47	37	56	45	36	52	42
Family history of Dislipidemia (%)	22	31	26	24	34	30	19	25	22	25	34	29	19	30	24	22	35	27
Family history of Diabetes (%)	31	37	33	32	38	35	28	32	30	31	36	33	31	37	33	33	42	37

Table 5. Association with obesity/overweight (yes vs no) of the considered cardiovascular risk factors in a multivariate analysis, adjusted for high waist circumference, gender, macroarea, fruit&vegetables and alcohol intake.

	OR	p	C.I. 95%
Age (years)	0.991	0.001	0.988-0.994
Smoking (yes vs no)	0.831	0.001	0.753-0.918
Diabetes (yes vs no)	1.320	0.001	1.219-1.429
Hypertension (yes vs no)	1.790	0.001	1.619-1.978
Hypercholesterolemia (yes vs no)	0.921	0.041	0.852-0.996
Hypertriglyceridemia (yes vs no)	1.167	0.001	1.082-1.259

Table 6. Association with high waist circumference (yes vs no) of the considered cardiovascular risk factors in a multivariate analysis, adjusted for obesity/overweight, gender, macroarea, fruit&vegetables and alcohol intake.

	OR	p	C.I. 95%
Age (years)	1.028	0.001	1.026-1.030
Smoking (yes vs no)	0.937	0.108	0.865-1.014
Diabetes (yes vs no)	1.345	0.001	1.251-1.452
Hypertension (yes vs no)	1.615	0.001	1.499-1.740
Hypercholesterolemia (yes vs no)	0.955	0.178	0.893-1.021
Hypertriglyceridemia (yes vs no)	1.324	0.001	1.240-1.413

Figure 1. Distribution of the cardiovascular risk factors in the study population according to gender

