Risk factors distribution and cardiovascular disease prevalence in the Italian population: The CHECK study

Elena Tragni¹, Alessandro Filippi², Manuela Casula¹, Giampiero Favato³, Ovidio Brignoli², Claudio Cricelli², Andrea Poli¹, Alberico L. Catapano¹,4* (for the CHECK Group#)

¹Epidemiology and Preventive Pharmacology Centre (SEFAP), University of Milano, Milano, Italy
²Italian Society of General Medicine (SIMG), Firenze, Italy
³Kingston University, Kingston upon Thames, UK
⁴IRCCS Multimedica, Sesto S. Giovanni, Milano, Italy
Email: *alberico.catapano@unimi.it

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ABSTRACT

Objective: To evaluate the distribution of cardiovascular risk factors and the prevalence of cardiovascular disease in a sample of the Italian population.

Methods: CHECK (Cholesterol and Health: Education, Control and Knowledge) is a cross-sectional observational study in a randomised sample of the Italian adult population aged 40 - 79 years, in the setting of general practice. Results: 5846 subjects (50.3% male) were included in the analysis. The mean age [±SD] of the observed cohort was 57.8 (±10.3) years. One out of five subjects smoked cigarettes and almost 80% didn’t engage in regular leisure-time physical activity. The mean blood pressure was 132.0 [±14.7]/81.2 [±7.9] mmHg. The total and LDL-cholesterol levels were respectively 205.3 [±35.9] mg/dL and 124.9 [±29.9] mg/dL. The mean glucose concentration was 98.3 [±28.2] mg/dL. The prevalence rate of hypertension, hypercholesterolemia, and type 2 diabetes were respectively 51.8%, 55.6%, and 13.0%. 8.9% of the observed subjects had a history of cardiovascular events, while in the primary prevention group the 10-year-risk of coronary heart disease (Framingham algorithm) was 10.1% [±8.3%] and of cardiovascular disease (CUORE algorithm) was 5.2% [±5.9%]. Conclusion: The CHECK study provides a detailed description of a randomised sample of the Italian population, contributing to evaluate the prevalence of cardiovascular risk factors and the main cardiovascular disease in Italy and to provide a baseline to set priorities and objectives for future intervention of health policy.

Keywords: Italian Population; Epidemiological Study; Cardiovascular Risk Factors; Prevalence of Cardiovascular Disease

1. INTRODUCTION

Cardiovascular diseases (CVD), a group of disorders of the heart and blood vessels, including coronary heart disease, cerebrovascular disease, peripheral arterial disease, are the leading cause of morbidity, disability and mortality worldwide, showing a continue increasing trend. In 2008, CVD caused 17 million deaths (47.2% of non-communicable diseases deaths, 29.8% of total deaths in the world) [1]; in particular, 7.6 million deaths were due to ischemic heart disease and 5.7 million to stroke [2].

CVD remains the first cause of death and disability in Italy although a slow and stepwise reduction of incidence has been observed since the mid seventies [3,4].

The subjects who survive acute cardiovascular events are likely to become chronic patients. CVD compromise patients’ quality of life and represent a significant economic burden to the national health system. Cardiovascular drugs account for about 26.4% of the Italian Pharmaceutical expenditure [5].

The CHECK (Cholesterol and Health: Education, Control and Knowledge) study was designed to provide information on the distribution of the main CVD risk factors in Italy setting the stage for addressing questions relative to the plausibility and feasibility of interventions on the principal risk factors for CVD in an European country.

CHECK is the first randomised Italian epidemiological study performed in primary care. Its main objective was to evaluate the distribution of cardiovascular risk factors and the prevalence of cardiovascular disease in a representative sample of the Italian adult population aged 40 - 79 years. Other aims were 1) to perform a follow-up study to determine the incidence of cardiovascular events...
and other main pathologies, 2) to create plasma and DNA banks to design ad-hoc nested case-control studies, 3) to disseminate information about cardiovascular risk factors to increase physicians and patients awareness and contribute to the implementation of evidences supporting health policies and preventive strategies in the population.

In this paper we describe baseline characteristics of enrolled subjects.

2. MATERIAL AND METHODS

The study was conducted in accordance to the Declaration of Helsinki, Guidelines for Good Clinical practice, and the Italian bioethics regulations and laws. The study was approved by the local Ethic Committee and all subjects gave written informed consent to the study (protocol code SEFAP/Pr. 0003).

2.1. Study Design

The Italian Society of General Medicine (SIMG) identified 54 general practitioners (coordinators) that were active at local level and distributed throughout the Italian territory (both rural and urban areas) in proportion to the regional population density. Each coordinator had to contact other general practitioners (GPs) who were operating on the same territory, to reach a group of 14 GPs.

Overall, 764 GPs were invited to participate to the study as investigators. They had to meet all the following pre-requisites:
- age: <52 years;
- practice size: >1000 subjects;
- computerised patient records system;
- access to the web.

The GPs who adhered to the proposal had to registered in the project website and to provide some personal information and their patients number. Each investigator was required to enrol 16 subjects aged 40 to 79 years, randomly selected among his patients, following a random number list generated by the coordinating Centre in Milan based on self-reported number of patients. The patient selection procedure was subject to random control by the local coordinators. Subjects who didn’t give their consensus or who were not eligible for practical reasons (e.g. subjects with walking disabilities, severe handicap, or suffering from an invaliding disease or a severe mental illness) were excluded from the randomized sample. The subjects’ enrolment started in March 2002 and ended in June 2005.

2.2. Data Collection

Subjects’ clinical history and clinical information were collected during a standardised visit performed by the investigating physician.

Information about smoking habit, physical activity, alcohol use and chronic drug treatments were collected directly from the patient during the same examination. Smoking habit was classified as current (patient smoking at least one cigarette per day) or former (at least one year from smoking cessation). Self-reported leisure-time physical activity was classified as present or non-present. The use of alcohol was evaluated by adding the consumption of red and/or white wine, beer and liquors. Information on chronic therapies was also collected.

Weight and height measures, obtained from lightly clothed patients, were expressed in terms of body mass index (BMI, weight in kilos divided by the square value of height, in meters).

The measurement of blood pressure (BP) was performed with the patient in sitting position, after 4 minute of rest, applying the appropriate cuff on the right arm. Systolic and diastolic blood pressure was identified at the beginning of the first and the fifth phase of the Korotkoff sounds, using a mercury sphygmomanometer with the appropriate cuff. Three consecutive readings were recorded and their mean was considered for the analysis. Heart rate was assessed as beats per minute after the last measurement of BP.

The presence of angina pectoris or of a history of myocardial infarction, coronary artery bypass graft or coronary angioplasty, stroke, transient ischemic attacks, claudicatio and left ventricular hypertrophy were assessed by retrieving the medical records of the subject and by direct inquiry. Subjects with a history of cardiovascular events (excluding left ventricular hypertrophy) were considered in secondary prevention.

Family history for premature cardiovascular diseases was determined when episodes of stroke and/or myocardial infarction were reported for one or more first-degree relatives, <55 years old for men and <65 years old for women. Family history for hypertension, dislipidemia, and diabetes was also evaluated.

All relevant subject records were entered in a computerized patient chart directly by the investigating physician and then sent to a central server via web.

Blood samples were drawn at the beginning of the enrolment visit. Blood was obtained between 8 to 10 am, from the antecubital vein, in sitting position, after 12 hours of fasting and alcohol abstinence. Blood samples were then collected in EDTA or monoiiodine-acetate (only for glucose assessment) coated tubes and shipped by courier at 4°C temperature to the central laboratory (Fleming SpA, in Brescia, Italy) within 24 hours, where the biochemical parameters were determined. The biochemical evaluation was performed following the criteria of the World Health Organization Lipid Reference Laboratories.
Upon arrival, the samples were centrifuged to obtain the plasma. Levels of total cholesterol (TC), glucose and triglycerides (TG) were measured by a chromatometric enzymatic method; the plasma levels of apolipoprotein B by a latex enhanced turbidimetric immuno-assay. Plasma HDL cholesterol levels (HDL-C) were measured after the precipitation of the apolipoprotein B containing lipoproteins with dextran-magnesium-chloride. All determinations were performed by an automatic analyzer (ADVIA 1650; Bayer, Germany). Fibrinogen plasma levels (1.8 - 3.5 g/L) were assessed by a turbidimetric method (VIA 1650; Bayer, Germany). Hypertriglyceridemia: plasma levels of TG ≥ 200 mg/dL or pharmacological treatment with statins and/or simvastatin + ezetimibe.

Hypertension: recorded diagnosis by physician or systolic BP ≥ 140 mm Hg or diastolic BP ≥ 90 mm Hg or currently taking medication to lower high BP (NHANES criteria [6]).

Type 2 diabetes mellitus: recorded diagnosis by physician or fasting blood glucose levels ≥ 170 mg/dL or currently taking antidiabetic drugs (oral hypoglycaemic medication and/or insulin).

Overweight: body mass index (BMI) ≥ 25 and <30 kg/m²;

Obesity: BMI ≥ 30 kg/m²;

Metabolic Syndrome (MetS): presence of at least 3 of the listed characteristics [7]: abdominal obesity, given as waist circumference, men > 102 cm, women > 88 cm; triglycerides ≥ 150 mg/dL; HDL cholesterol, men < 40 mg/dL, women < 50 mg/dL; blood pressure ≥ 130/85 mmHg; fasting glucose ≥ 110 mg/dL. BMI was used as a surrogate of waist circumference, men ≥ 28 kg/m², women ≥ 25 kg/m² (approach validated in a subgroup of about 1000 subjects: assignment to MetS/noMetS consistent in 92% of cases in males and 97% in females).

The coronary heart disease risk (CHD risk % in 10 years) was calculated using the Framingham algorithm [8], as recommended at the time of the study by the Italian regulatory Agency (AIFA) for the prescription of statin drugs [9]; the global cardiovascular risk (CVD risk % in 10 years) was evaluated using the CUORE algorithm [10], developed from epidemiological data obtained in Italy, as reported by Italian recommendations since 2003 [11]. Based on Framingham or CUORE scores, subjects were stratified in four risk classes (<5% low-risk; 5% - 10% mild-risk; 10% - 20% moderate-risk; ≥20% high risk).

2.3. Statistical Analysis

Normally distributed variables are presented as mean values [± standard deviation, SD] and not normally distributed variables as median [interquartile range, IQR], while qualitative variables are presented as frequencies. Comparisons between continuous variables across sex groups were performed by using the t-test for independent sample. Comparisons between proportions across sex groups for categorical and qualitative variables were performed by using non-parametric tests. All reported p-values are based on two-sided tests and compared to a significance level of 5%.

All statistical analyses were performed using the Windows 16.0 version of SPSS (SPSS, Inc., Chicago, Illinois).

3. RESULTS

432 GPs participated to the CHECK study (mean age 47.8 years, 80.1% male; 56.5% participation rate). Each of them enrolled up to 16 subjects, following the randomised sampling procedure. Overall, 6890 subjects were enrolled; 1044 (15.1%) of them did not attend the medical visit and were excluded from the study sample; the blood samples of 131 subjects (1.9%) were not processable, although their anamnestic data were included in the analysis.

5846 subjects were included in the final analysis (Figure 1). Men were 49.7% of the cohort. The mean age was 57.8 years (58.2 years for men and 57.4 for women). Comparison between the Check demographics and the latest available census data [12] showed small difference: women were slightly under-represented in the CHECK sample (50.3% vs. 52.6% respectively); the 50 - 59 and 60 - 69 age groups, conversely, were slightly over-represented (30.5% vs. 27.0% and 28.0% vs. 24.6%, respectively).

The main outcomes of the study are shown in Tables 1-4. The average level of education is quite low: 33.0% of subjects achieved only primary education, but this percentage was higher in women (36.7% vs. 29.2%). 32.9% reported to be retired, with a high proportion of men (65.8%); 23.3% were housewives (45.8% of the female sample). Smoke habit and alcohol consumption were more prevalent in men (24.3% vs. 18.6% and 62.4% vs. 28.4%, respectively), whereas physical inac-
activity was more present in women (84.1% vs. 75.0%) (Table 1).

Mean BMI (±SD) was 26.5 ± 4.3 kg/m², putting the sample in the overweight range; this was observed in both genders. Mean SBP/DBP values were (132.0 ± 14.7)/(81.2 ± 7.9) mm Hg, slightly higher than cut off for pre-hypertension. Mean total cholesterol was 205.3 ± 35.9 mg/dL, while LDL-cholesterol was 124.9 ± 29.9 mg/dL, the former just higher and the latter slightly lower than desirable levels, due to HDL-cholesterol values (54.8 ± 12.2 mg/dL) (Table 2).

As shown in Table 3, 51.8% of subjects were hypertensive, 13.0% were diabetic, and 55.6%/20.8% were hypercholesterolemic/hypertriglyceridemic. 8.6% had a history of cardiovascular events and thus could be defined as in secondary CV prevention. The 65.0% of the remaining subjects had a global CV risk in 10 years (calculated with CUORE algorithm) lower than 5%, with a remarkable difference between genders (mean values: 7.8% ± 7.1% in men vs. 2.8% ± 3.1% in women) (Table 4).

4. DISCUSSION

The main objective of the CHECK study was to evaluate the cross-sectional prevalence of CVD and cardiovascular risk factors in a cohort of randomly selected Italian subjects, aged 40 to 79 years.

The CHECK sample proved to be representative of the Italian population in the same age range. The differences observed by comparing the CHECK demographics to the latest available census data [12] are small, and of limited relevance. This was probably due to a larger participation to the study of subjects in a non-working age or condition.

The CHECK study provided a detailed and in depth description of the prevalence of cardiovascular risk factors and the main cardiovascular pathologies in the Italian population. In order to put our findings into a wider context, we compare them with other national surveys, while maintaining a worldwide perspective.

Smoking is estimated to cause nearly 10% of cardiovascular disease (5.4 millions of deaths) [13]. Currently, there are about 1 billion smokers worldwide [14]. The proportion of smoking subjects in the CHECK sample was 21.4% (men 24.3% and women 18.6%). These figures were slightly lower than the official census data (24.5% in 2003, 22.6% in 2004) [15]; the Check cohort excluded the 25 - 34 age group, the one with the highest prevalence of smokers (31.4%), especially among men. The reduced prevalence of smokers in the CHECK cohort, as compared to previous epidemiological data [16], could also reflect the declining smoking habits in the Italian population, as a result of educational programs and smoking restrictions enforced in public buildings.

Physical inactivity is one of the leading risk factors for mortality and is estimated to cause about 30% of ischaemic heart disease burden [13]. Globally, around 31% of adults are insufficiently active (men 28% and women 34%) [17]. Concerning leisure-time physical activity, the self-reported information obtained from the CHECK cohort were less favourable than the data derived from other studies. The prevalence of physical inactivity was 75% in men and 84% in women, vs. 34% in men and 46% in women observed, as an example, in the Atlante study [18].

Overweight and obesity lead to adverse metabolic effects on blood pressure, cholesterol, triglycerides and insulin resistance [13]; all over the world, 2.8 million people die each year as a result of being overweight [13]. A total of more than half a billion adults worldwide are obese [19]. The mean BMI of the CHECK cohort was 26.5 kg/m², well within the overweight range. 17.4% of the cohort subjects were obese, with a higher prevalence in women than in men (18.8% vs. 16.0%, respectively). In the PASSI study, a national survey (self-reported information) conducted on younger people aged 18 - 69 years [20], 32% of Italians are overweight, while one in ten is obese [21].

Raised blood pressure is the leading risk factor for cardiovascular disease mortality, causing more than 7 million deaths every year worldwide. Globally, prevalence of hypertension in adults is around 40% [13]. In our study, the mean blood pressure value was 132.0/81.2 mmHg. Hypertension was present in more than half of the sample, with a higher prevalence in men (54.1% M vs. 49.5% W). The CHECK mean SBP values were comparable to those obtained in other Italian observational
### Table 1. Sociodemographic and lifestyle characteristics in total and sex-stratified sample.

<table>
<thead>
<tr>
<th></th>
<th>Total sample</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Subjects, n (%)</strong></td>
<td>5846</td>
<td>2903 (49.7)</td>
<td>2943 (50.3)</td>
</tr>
<tr>
<td><strong>Age, mean ± SD ((^\circ))</strong></td>
<td>57.8 ± 10.3</td>
<td>58.2 ± 10.1</td>
<td>57.4 ± 10.5</td>
</tr>
<tr>
<td><strong>Age distribution, N (%)(^\circ)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>40 - 49 years</td>
<td>1517 (26.0)</td>
<td>689 (23.7)</td>
<td>828 (28.1)</td>
</tr>
<tr>
<td>50 - 59 years</td>
<td>1784 (30.5)</td>
<td>912 (31.4)</td>
<td>872 (39.6)</td>
</tr>
<tr>
<td>60 - 69 years</td>
<td>1638 (28.0)</td>
<td>844 (29.1)</td>
<td>794 (27.0)</td>
</tr>
<tr>
<td>70 - 79 years</td>
<td>907 (15.5)</td>
<td>458 (15.8)</td>
<td>449 (15.3)</td>
</tr>
<tr>
<td><strong>Occupational status, N (%)(^\circ)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Employed</td>
<td>2109 (36.5)</td>
<td>1360 (47.4)</td>
<td>749 (25.8)</td>
</tr>
<tr>
<td>Housewife</td>
<td>1347 (23.3)</td>
<td>14 (0.5)</td>
<td>1333 (45.8)</td>
</tr>
<tr>
<td>Retiree</td>
<td>1902 (32.9)</td>
<td>1252 (43.7)</td>
<td>650 (22.3)</td>
</tr>
<tr>
<td>Unemployed</td>
<td>51 (0.9)</td>
<td>33 (1.2)</td>
<td>18 (0.6)</td>
</tr>
<tr>
<td>Other</td>
<td>367 (6.4)</td>
<td>207 (7.2)</td>
<td>160 (5.5)</td>
</tr>
<tr>
<td><strong>Educational level (highest degree), N (%)(^\circ)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>98 (1.7)</td>
<td>37 (1.3)</td>
<td>61 (2.1)</td>
</tr>
<tr>
<td>Elementary</td>
<td>1905 (33.0)</td>
<td>836 (29.2)</td>
<td>1069 (36.7)</td>
</tr>
<tr>
<td>Junior high</td>
<td>1840 (31.9)</td>
<td>916 (32.0)</td>
<td>924 (31.8)</td>
</tr>
<tr>
<td>High school</td>
<td>1488 (25.8)</td>
<td>808 (28.2)</td>
<td>680 (23.4)</td>
</tr>
<tr>
<td>University</td>
<td>445 (7.7)</td>
<td>269 (9.4)</td>
<td>176 (6.0)</td>
</tr>
<tr>
<td><strong>Life habits, N (%)(^\circ)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smokers</td>
<td>1253 (21.4)</td>
<td>706 (24.3)</td>
<td>547 (18.6)</td>
</tr>
<tr>
<td>Regular exercise</td>
<td>1181 (20.4)</td>
<td>717 (25.0)</td>
<td>464 (15.9)</td>
</tr>
<tr>
<td>Alcohol users</td>
<td>2613 (45.2)</td>
<td>1788 (62.4)</td>
<td>825 (28.4)</td>
</tr>
</tbody>
</table>

*Men vs. women (t-test) p = 0.003; \(^\circ\)Men vs. women (non-parametric tests) p < 0.05.

### Table 2. Anthropometric, vital and biochemical parameters in total and sex-stratified sample, mean ± SD.

<table>
<thead>
<tr>
<th></th>
<th>Total sample</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Height (m)</strong></td>
<td>N = 5843</td>
<td>1.65 ± 0.09</td>
<td>1.71 ± 0.07</td>
</tr>
<tr>
<td><strong>Weight (kg)</strong></td>
<td>N = 5835</td>
<td>72.5 ± 13.4</td>
<td>78.5 ± 11.7</td>
</tr>
<tr>
<td><strong>BMI (Kg/m(^2))</strong></td>
<td>N = 5835</td>
<td>26.5 ± 4.3</td>
<td>26.9 ± 3.5</td>
</tr>
<tr>
<td><strong>SBP (mmHg)</strong></td>
<td>N = 5844</td>
<td>132.0 ± 14.7</td>
<td>133.0 ± 13.8</td>
</tr>
<tr>
<td><strong>DBP (mmHg)</strong></td>
<td>N = 5844</td>
<td>81.2 ± 7.9</td>
<td>81.9 ± 7.8</td>
</tr>
<tr>
<td><strong>Heart rate (bpm)</strong></td>
<td>N = 5773</td>
<td>73.3 ± 8.5</td>
<td>72.6 ± 8.5</td>
</tr>
<tr>
<td><strong>TC (mg/dL)</strong></td>
<td>N = 5710</td>
<td>205.3 ± 35.9</td>
<td>202.5 ± 35.7</td>
</tr>
<tr>
<td><strong>HDL-C (mg/dL)</strong></td>
<td>N = 5710</td>
<td>54.8 ± 12.2</td>
<td>50.7 ± 10.4</td>
</tr>
<tr>
<td><strong>TG (mg/dL)</strong></td>
<td>N = 5710</td>
<td>132.8 ± 102.1</td>
<td>149.9 ± 120.6</td>
</tr>
<tr>
<td><strong>LDL-C (mg/dL)(^\circ)</strong></td>
<td>N = 5614</td>
<td>124.9 ± 29.9</td>
<td>123.3 ± 29.3</td>
</tr>
<tr>
<td><strong>ApoB (mg/dL)</strong></td>
<td>N = 5710</td>
<td>111.4 ± 25.2</td>
<td>112.5 ± 25.3</td>
</tr>
<tr>
<td><strong>Non-HDL-C (mg/dL)(^\circ)</strong></td>
<td>N = 5710</td>
<td>150.5 ± 33.8</td>
<td>151.8 ± 33.6</td>
</tr>
<tr>
<td><strong>Glucose (mg/dL)</strong></td>
<td>N = 5547</td>
<td>98.3 ± 28.2</td>
<td>101.7 ± 29.6</td>
</tr>
<tr>
<td><strong>Fibrinogen (g/L)</strong></td>
<td>N = 5710</td>
<td>3.41 ± 0.69</td>
<td>3.34 ± 0.70</td>
</tr>
</tbody>
</table>

BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; TC: total cholesterol; TG: triglycerides; apoB: apolipoprotein B; \(^\circ\)Men vs women (t-test) p = 0.01 for all comparisons; \(^\circ\)Obtained by the Friedewald formula; \(^\circ\)TC – (HDL-C).
Table 3. Prevalence of cardiovascular disease and related comorbidities in total and sex-stratified sample, N (%).

<table>
<thead>
<tr>
<th>Comorbidities</th>
<th>Total sample</th>
<th>Men</th>
<th>Women</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension*</td>
<td>N = 5774</td>
<td>2990  (51.8)</td>
<td>1549 (54.2)</td>
<td>1441 (49.5)</td>
</tr>
<tr>
<td>Hypercholesterolemia*</td>
<td>N = 5707</td>
<td>3172  (55.6)</td>
<td>1514 (53.5)</td>
<td>1661 (57.9)</td>
</tr>
<tr>
<td>Hypertriglyceridemia*</td>
<td>N = 5707</td>
<td>1191  (20.8)</td>
<td>780 (27.8)</td>
<td>411 (14.5)</td>
</tr>
<tr>
<td>Mixed dyslipidemia*</td>
<td>N = 5707</td>
<td>935   (14.8)</td>
<td>598 (21.3)</td>
<td>337 (11.9)</td>
</tr>
<tr>
<td>DM2°</td>
<td>N = 5568</td>
<td>723   (13.0)</td>
<td>432 (15.6)</td>
<td>291 (10.4)</td>
</tr>
<tr>
<td>Obesity</td>
<td>N = 5853</td>
<td>1011  (17.3)</td>
<td>463 (16.0)</td>
<td>552 (18.8)</td>
</tr>
<tr>
<td>Metabolic syndrome</td>
<td>N = 5660</td>
<td>1306  (23.1)</td>
<td>629 (22.3)</td>
<td>677 (23.8)</td>
</tr>
</tbody>
</table>

Cardiovascular events

<table>
<thead>
<tr>
<th></th>
<th>Total sample</th>
<th>Men</th>
<th>Women</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stable angina</td>
<td>N = 5846</td>
<td>113   (1.9)</td>
<td>68 (2.3)</td>
<td>45 (1.5)</td>
</tr>
<tr>
<td>Unstable angina</td>
<td>N = 5846</td>
<td>74    (1.3)</td>
<td>48 (1.7)</td>
<td>26 (0.9)</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>N = 5846</td>
<td>180   (3.1)</td>
<td>154 (5.3)</td>
<td>26 (0.9)</td>
</tr>
<tr>
<td>CABG</td>
<td>N = 5846</td>
<td>46    (0.8)</td>
<td>39 (1.3)</td>
<td>7 (0.2)</td>
</tr>
<tr>
<td>PTCA</td>
<td>N = 5846</td>
<td>76    (1.3)</td>
<td>65 (2.2)</td>
<td>11 (0.4)</td>
</tr>
<tr>
<td>Transient ischemic attack</td>
<td>N = 5846</td>
<td>118   (2.0)</td>
<td>71 (2.4)</td>
<td>47 (1.6)</td>
</tr>
<tr>
<td>Ischemic stroke</td>
<td>N = 5846</td>
<td>41    (0.7)</td>
<td>25 (0.9)</td>
<td>16 (0.5)</td>
</tr>
<tr>
<td>Claudicatio</td>
<td>N = 5846</td>
<td>82    (1.4)</td>
<td>73 (2.5)</td>
<td>9 (0.3)</td>
</tr>
<tr>
<td>Secondary prevention</td>
<td>N = 5846</td>
<td>501   (8.6)</td>
<td>354 (12.2)</td>
<td>147 (5.0)</td>
</tr>
<tr>
<td>LVH</td>
<td>N = 5846</td>
<td>526   (9.0)</td>
<td>288 (9.9)</td>
<td>238 (8.1)</td>
</tr>
</tbody>
</table>

Family history

<table>
<thead>
<tr>
<th></th>
<th>Total sample</th>
<th>Men</th>
<th>Women</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coronary heart disease</td>
<td>N = 5846</td>
<td>681    (11.6)</td>
<td>323 (11.1)</td>
<td>358 (12.2)</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>N = 5846</td>
<td>454    (7.8)</td>
<td>205 (7.1)</td>
<td>249 (8.5)</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>N = 5846</td>
<td>1579   (27.0)</td>
<td>763 (26.3)</td>
<td>816 (27.7)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>N = 5846</td>
<td>2897   (49.6)</td>
<td>1346 (46.4)</td>
<td>1551 (52.7)</td>
</tr>
<tr>
<td>DM2</td>
<td>N = 5846</td>
<td>1542   (26.4)</td>
<td>740 (25.5)</td>
<td>802 (27.3)</td>
</tr>
</tbody>
</table>

DM2: type 2 diabetes mellitus; CABG: coronary artery bypass graft surgery; PTCA: percutaneous transluminal coronary angioplasty; LVH: left ventricular hypertrophy; NS: not significant; *Criteria used for specific diagnosis are described in Methods paragraph; †Criteria for definition are described in Methods paragraph; ‡Men vs. women (non-parametric tests).

Table 4. CHD-risk classes and CVD-risk classes in total and sex stratified sample.

<table>
<thead>
<tr>
<th></th>
<th>Framingham</th>
<th>CUORE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk %, mean ± SD†</td>
<td>10.1 ± 8.3</td>
<td>5.2 ± 5.9</td>
</tr>
<tr>
<td>Risk classes, n (%)§</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;5.0%</td>
<td>1415 (30.8)</td>
<td>2736 (65.0)</td>
</tr>
<tr>
<td>5.0% - 9.9%</td>
<td>1420 (30.9)</td>
<td>858 (20.4)</td>
</tr>
<tr>
<td>10.0% - 19.9%</td>
<td>1257 (27.3)</td>
<td>470 (11.2)</td>
</tr>
<tr>
<td>&gt;=20.0%</td>
<td>505 (11.0)</td>
<td>142 (3.4)</td>
</tr>
</tbody>
</table>

†Values calculated within the limits of each algorithm; ‡Men vs. women (t-test) p < 0.001; §Men vs. women (non-parametric tests) p < 0.001.
plasma glucose levels
98.3 mg/dL (101.7 M vs. 94.9 W). Based on GPs diag-
oence of diabetes is estimated to be 10% [13]. In the
sequences of high blood sugar [24]. The global preva-
disease and cardiovascular disease [23]. A 2004 survey
showed that more than 3 million people died from con-
ally burden as a risk factor for ischaemic heart disease and
stroke. Overall, it is estimated to cause 2.6 million deaths
(4.5% of total). The global prevalence of hypercholes-
terolemia among adults is about 39% [13]. The mean
plasma total cholesterol levels in the CHECK cohort
were 205.3 mg/dL. The prevalence of hypercholes-
terolemia was 55.6%. Hypertriglyceridemia and mixed
dyslipidemia were identified in 20.8% and 14.8% of the
enrolled subjects, respectively. Lipid data observed in
the CHECK and in the Atlante study showed relevant simi-
larities: in both cohorts, women showed a higher level of
TC, LDL-C, and HDL-C than the same level reported for
men, but lower TG values. TC mean values observed in
the CUORE population [22], on the other hand, were sig-
nificantly higher than those found in CHECK (CUORE
225.4 mg/dL M and 229.0 mg/dL W vs. CHECK 202.5
mg/dL M and 208.0 mg/dL W). This difference is con-
sistent with the trend of progressive reduction of blood
TC levels observed over the last decades in Italy.

Impaired glucose tolerance and impaired fasting gly-
caemia are risk categories for future development of
diabetes and cardiovascular disease [23]. A 2004 survey
showed that more than 3 million people died from con-
sequences of high blood sugar [24]. The global preva-
ience of diabetes is estimated to be 10% [13]. In the
CHECK cohort, the mean level of fasting glucose was
98.3 mg/dL (101.7 M vs. 94.9 W). Based on GPs diag-
nosis and/or presence of anti-diabetes therapies and/or
plasma glucose levels ≥ 126 mg/dL, type II diabetes
prevalence was 13.0%. This prevalence was higher than
that observed in the Health Search GP’s database of Ital-
ian general practice [25] for similar age (10% - 11%;
unpublished observation). This difference can be par-
tially explained by different diagnostic criteria (based on
at least two assessments in clinical practice compared to
the single time determination in the CHECK study pro-
tocol), or by the identification of previously unknown
cases in the CHECK sample, due to the generalised
screening. In the Atlante cohort, the mean fasting glu-
cose levels was lower (93 mg/dL M vs. 87 mg/dL W),
leading to a lower prevalence of type II diabetes (Atlante
9% M and 6% W vs. CHECK 15.6% M and 10.4% W).
This difference could be partially explained by the dif-
ferent timeframe of the two studies (Atlante from 1998
vs. CHECK from 2001): over the last years, a general-
ised increase in the prevalence of type II diabetes in
Western populations has been observed. Moreover, in the
Atlante study the blood glucose level was estimated from
a sample of capillary blood, where glucose concentra-
tions are on average significantly lower than in plasma.

Cardiovascular disease is the number one cause of
death globally. In Italy, an estimated almost 240,000
people died from CVDs in 2008, representing 41% of all
total deaths [26]. A clinical history of previous cardio-
vascular events was observed in 8.6% of the individuals
included in the CHECK sample. The prevalence of such
diagnosis was twice as high in men than in women. The
prevalence of a clinical history of myocardial infarction
was higher in the CHECK than in the Atlante study, es-
pecially in men (CHECK 5.3% M and 0.9% W vs. At-
lante 1.5% M and 0.4% W). The difference could be
explained by the different methodological approach (in-
formation collected in a GP interview vs. hospital valida-
tion) and age differences.

The risk of future fatal and non-fatal cardiovascular
events was assessed using two different algorithms,
based on the outcomes of the Framingham and the Cuore
cohorts. The mean coronary risk at 10 years, calculated
with the Framingham algorithm, was 10.1%, while the
cardiovascular risk calculated with the CUORE algo-

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tions, previously described. Importantly, the prevalence of cardiovascular events could have been underestimated, as the participating general practitioners reported those events at best of their knowledge, simply transcribing the diagnose related groups (DRG) codification of the events as reported by the hospital discharge letter, without any form of control on the appropriateness of the diagnoses. In addition, the peculiar design of the study, with progressive steps of GPs involvement, determined a participation rate lower than expected. The fact that local investigators did not participate in the enrolment meetings with the coordinating Centre, but were trained by their coordinators, may have weakened their motivation. However, no significant differences have been found between actively participating GPs and those who did not complete the preliminary steps.

5. CONCLUSIONS

The CHECK study confirmed the significant burden caused by the cardiovascular disease to the health care system and to society. In the randomised cohort observed, 1 out of 2 subjects was suffering from high blood pressure or high cholesterol, 1 out of 5 was obese and 1 out of 10 was a type 2 diabetic. The elevated prevalence of lifestyle risk factors observed in the Italian population raises the issue of moral hazard: the limited willingness of subjects covered by the National Healthcare System to take action and modify behavioural risks, in favour of deferring the issue to pharmacological prevention or treatment of the cardiovascular events at a later stage. While this normative issue is well known in economics of public health, the CHECK findings on the prevalence and co-occurrence of key behavioural and clinical risk factors is an emerging concern and it demands further research. Despite the fact that most subjects included in the study had been followed-up by general practitioners for years, the vast majority of them still showed the presence of one or more risk factors.

The high proportion of subjects with multiple risk factors in combination with the elevated prevalence of cardiovascular disease projects a shadow on the effectiveness of current cardiovascular prevention policies in primary care. The epidemiological outcomes of this study could be used as a baseline to set priorities and objectives for future intervention, as well as a benchmark, against which the effectiveness of the implementation of future prevention policies in primary care should be measured. The further development of the CHECK study is aimed to facilitate the recognition and to improve the management of cardiovascular diseases in the Italian general practice.

6. ACKNOWLEDGEMENTS

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REFERENCES


Appendix

Participating Investigators in the CHECK Study Group (Bold Type for Coordinators)

Boccone Nicolfreando
Boito Giancarlo
Bolso Alberto Maria
Boncompagni Salvatore
Bond Giuseppe
Bonetti Maria Grazia
Bon Giafranco
Boscaro Federica
Bosso Paolo
Bozza Giulio
Bracone Enrico
Brandtodorlucio
Brascesco Pierladuro
Breviario Adele
Brizzi Antonio
Brugnetta Maurizio
Bruno Giuseppe
Buemi Giuseppe
Bufano Camarina
Bugli Tiziano
Burigo Daniela
Buzzatti Agostino
Caccamo Orazio Antonio
Cadamosti Danilo
Cagliesi Francesco
Calefia Manuela
Cammissa Nicola
Campo Francesco
Campobello Margherita
Caputo Stanislao
Caracci Nicola
Card Silvio
Cardinale Fulvio
Carena Maximo
Cariola Gianni
Carlino Saverio
Carminati Luisa Angela
Carnelli Feliciano
Cassarino Francesco
Caruso Ciro
Casale Ezio
Casini Marcella
Cassanelli Marco
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Castriotta Antonio
Catalano Domenico
Cataldi Maria Elvia
Ceccarini Agostino
Celebrano Mario
Celora Amedeo
Cerracchio Alessandro
Cesaro Andrea
Cesaro Federico
Chirivati Alberto
Cipriani Rosa
Culla Giuseppe
Colombo Valter
Colaccia Salvatore
Conte Sergio
Corda Andrea
Costa Roberto
Cottani Antonio
Crivellenti Giuseppe
D’Ambrosio Gaetano
D’Angelo Massimo
Dalla Rosa Rosanna
Damiano Gianantonio
De Andreis Besso Pier Luigi
De Benedetiches Antonio
De Conto Umberto
De Mola Cosimo
De Rosa Antonio
De Tommasi Roberto
Del Nero Barbara
Della Brido Livana
Dell’Orco Mario Domenico
Dell’Orco Mario Lucio
Di Candia Giuseppe
Di Carlo Vittorio
Di Feo Enrico
Di Feo Andino
Di Fraia Giovanni
Di Fulvio Aristide
Di Nardo Dionisio
Dolometta Franco
Donzelli Luigi
Dughiero Fausto
Durando Andrea
Ercolino Luigi
Fabbrini Stefania
Fabrizio Nicola
Falchi Raffaello
Farnello Ciro
Fascendini Emilvio
Fasulo Serenella
Federici Laura
Ferioli Paola
Ferrari Vincenzo
Fidelio Melchiore
Filetti Giuseppe
Filippini Giovanni
Fogher Michele
Franchini Carlo Andrea
Frascato Angelo
Frinaglia Patrizia
Fronteppiero Francesco
Gadaleta Califaloro Gennaro
Galantini Giovanna
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Gerace Antonio
Geremia Maria Alessandra
Germi Fabrizio
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Invernizzi Giovanni
Iocca Tommaso
Kos Egidia
La Mattina Rosolina
La Torre Angelo
Lacava Cosimo
Lalli Pasqualino
Lamer Giorgio
Lanza Gerardo
Lardino Gerardo
Laringe Matteo
Lattanzio Giuseppe
Le Foche Luca
Leo Rosanna
Leuzzi Giacomo
Lipari Antonino
Lipari Francesco
Lippa Luciano
Lo Conte Maurizio
Lo Giudice Domenico
Lonati Rossella
Lorenzina Enrico
Magi Lorenzo
Magliozzo Francesco
Manallano Luciano
Mantovanie Lucia
Marcenaro Alessandro
Marchetti Anna Rosa
Marino Carla
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Marti Ronchi
Maschi Giulio
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Morganti Mauro
Mormile Severo
Morrone Annarita
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