



Original article

Risk factors for cardiovascular disease in Sardinia from 1978 to 2001: A comparative study with Italian mainland

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ABSTRACT

Background: This study is a survey of cardiovascular risk factors in Sardinia in the years 1999–2001 and allows us to update previously observed trends of such factors and to compare them with those in the Italian mainland.

Methods: Random samples of free living population of the Mediterranean island of Sardinia, Italy, were collected. Overall, 6818 subjects, 50% of each sex, and aged 20–80+ years constituted the sample. Personal and family data were collected using a semiquantitative questionnaire of frequencies. Blood biochemical variables related to risk for atherosclerosis were measured. In particular, serum total cholesterol, HDL-cholesterol, triglycerides, Apo A-1, Apo B, Lp(a), uric acid, blood glucose and plasma homocysteine were analyzed in each subject enrolled.

Results: In the age classes 20–59 years, during a 30 year period, prevalence of smoking among males continued to decrease from 58 to 24% (p for trend <0.001), and, for the first time, prevalence of smoking among females decreased as well: from 31% in 1995 to 20% in 2001 (p for trend <0.001). In contrast, a steady increase in TC (mg/dl) (189, 206, 215, 216, p for trend <0.05 in males and 184, 197, 212, 217, p for trend <0.05 in females), and LDL-C (136, 143, 138, 144, p for trend <0.05 in males and 127, 139, 136, 135, p for trend <0.05 in females) was observed. HDL-C showed a steady increase (p for trend <0.01 in males and females). Lp(a) values were high in both sexes, a finding linked to the ethnic influence on them. Systolic and diastolic blood pressure values (mm Hg) increased with age. In the present survey (population aged 20–80+ years, current smokers were 17.5% among males and 13.8% among females. Total and HDL-cholesterol were higher than in other parts of Italy (209 vs 205 in males, and 211 vs 204 in females), while systolic and diastolic blood pressure were lower.

Conclusion: Overall, total- and LDL-cholesterol showed an increasing trend, while blood pressure and smoking habits had a decreasing tendency. The increase in blood cholesterol follows the trend in other areas of the world, mainly due to changing dietary habits. Therefore, a campaign of eating information and education (population strategy) could favourably modify cardiovascular risk, as occurred in Sardinia during the past decade with the Regional ATS-Sardegna Campaign.

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Abbreviations: Apo A-1, Apolipoprotein A-1; Apo B, Apolipoprotein B; BMI, Body mass index; CVD, Cardiovascular disease; Diast, Diastolic blood pressure; G, Blood glucose; H, Hip circumference; HCY, Homocysteine; HDL-C, High-density lipoprotein cholesterol; LDL-C, Low-density lipoprotein cholesterol; Lp(a), Lipoprotein(a); Syst, Systolic blood pressure; TC, Total cholesterol; TG, Triglycerides; WC, Waist circumference; W/H, Waist/Hip ratio; 80+, 80 years of age and over.

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1. Introduction

Cardiovascular disease (CVD), i.e. coronary heart disease (CHD), stroke, and peripheral vascular disease, are potentially preventable diseases. Thanks to epidemiological, experimental and clinical studies, the primary determinants of CVD have been identified, as well as the efficacy of specific interventions. The prevalence of cardiovascular disease is increasing in less urbanized, developed populations across the world, as their lifestyles change to a so called “western style”, with increasing consumption of dietary saturated fat, cholesterol and salt, cigarette smoking, decreased physical activity and the rise in CVD risk factors including obesity and diabetes [1]. Other known factors that

Table 1

Population samples (each made of 50% males and 50% females, aged 20–80+ years) randomized in the four communes, and their participation (number and percentage) in the survey 1999–2001.

	Random sample	Participants (n)	Participation (%)
Ploaghe	1960	1504	76.73
Sorso	1232	795	64.53
Sinnai	2408	1784	74.00
Maracalagonis	1218	654	53.69
Total	6818	4737	69.48
Males		2250 (47.5%)	
Females		2487 (52.5%)	
Total		4737 (100.0%)	

contribute to CVD risk are stress [2] and high alcohol intake [3]. Among all these factors, hypercholesterolemia is the leading cause of death from CHD. As a result, public health agencies have attempted to reduce the prevalence of hypercholesterolemia through screening and by increasing public awareness and strategies for reducing it [4].

Over the past two decades, the mean population values of blood pressure, total cholesterol and the prevalence of current smoking has been decreasing in the UK [5] and in Finland [6], although the situation is far from optimal.

In the WHO MONICA Project, cigarette smoking decreased between 1980 and the mid-1990s for men by more than 5% (except in China) due to higher proportion of never smokers in the younger age groups, rather than to quitting smoke. For women, smoking tended to increase in populations with low prevalence, and decrease in populations with higher prevalence [7].

Body mass index (BMI) increased more rapidly among adults of low socioeconomic status. In both sexes BMI increased by 0.19 annually in the UK [5].

In the Mediterranean island of Sardinia, mean levels and distribution of CVD risk factors have been monitored from 1978 to 2001 in random samples of free living population, and compared with those from other Italian regions [8–14]. In 1978 plasma cholesterol levels in Sardinians had the lowest values among the Italian population [8]. The present paper deals with the last survey we carried out in Sardinia around the year 2000 (1999–2001), with financial support from the Sardinian Government [15], so allowing a completion of data recorded and comparison with the trends of the same risk factors in the rest of Italy [16].

2. Materials and methods

2.1. Design and study period

This was a study population survey performed during years 1999–2001 in Sardinia, an insular region of Italy, under promotion and with financial support from the Sardinian Government [15].

2.2. Study population

Random samples of free living population were drawn from the municipal lists of northern (Ploaghe and Sorso) and southern (Sinnai and Maracalagonis) communes. Overall, 6818 subjects, 50% of each sex, and aged 20–80+ years constituted the sample with a participation rate of 69.48%, thus making 4737 examined, of whom 2250 males and 2487 females (Table 1).

2.3. Variables

Systolic and diastolic BP were measured and diagnosis of high blood pressure was made when systolic was ≥ 140 and diastolic ≥ 90 mm Hg [17].

Impaired fasting glycemia was diagnosed if glucose was ≥ 110 mg/dl (it was evaluated before it was lowered to ≥ 100 mg/dl) and < 126 mg/dl (≥ 6.10 and < 7.00 mmol/L) and diabetes if glucose was ≥ 126 mg/dl (7 mmol/L) [18].

Hypercholesterolemia was diagnosed when serum cholesterol level was > 200 mg/dl (5.20 mmol/L); Hypertriglyceridemia when serum triglycerides were ≥ 150 mg/dl (1.7 mmol/L); Hyper-LDL-cholesterol when serum LDL was ≥ 130 mg/dl (3.38 mmol/L) [19].

Hypo-HDL-cholesterolemia was diagnosed when serum HDL was < 40 mg/dl (1.04 mmol/L) [19]. In the context of metabolic syndrome, low HDL-cholesterol is < 40 mg/dl for men and < 50 mg/dl for women [19].

Apolipoproteins were measured according to Standardization Project Guidelines [20].

HyperLp(a) was diagnosed when serum levels exceeded 30 mg/dl [21].

Homocysteinemia was characterized by plasma levels exceeding 12 $\mu\text{mol/L}$ for both sexes [22,23].

Body mass index (BMI) ≥ 30 kg/m² was considered indicative of obesity.

A semiquantitative food frequency questionnaire formerly used in National Research Council (CNR) and ATIS-Sardegna surveys [13] was administered in order to investigate dietary habits.

Current daily smoking or having quit within the previous 6 months characterized smokers.

Alcohol abuse was defined by daily drinking of more than 3 drinks in males and 2 drinks in females. Under these values, alcohol consumption was considered “normal” (mainly wine during meals).

The use and type of drugs were monitored.

2.4. Ethical aspects

The study complies with the Declaration of Helsinki. The Sardinian Government promoted and financed it [15]. All participants were informed of the study objective and gave written informed consent.

2.5. Statistical methods

When comparing the mean values of classical risk factors for CVD with those recorded in the surveys from 1978 to 2001, the population samples were restricted to 20–59 years of age. To evaluate the association of categorical variables, we used the chi-square test (χ^2); *p* values below 0.05 were considered statistically significant. Differences between mean values of population samples examined in different periods or in different areas were tested by the unpaired *t* test, except for the prevalence of smoking, which was tested by the test of proportions.

Standardization for age (males and females independently) has been made by the direct method, taking as the reference population

Table 2

Prevalence (%) of current smokers by sex and age in 1984 and 2001.

Age-class (years)	Males		Females	
	1984	2001	1984	2001
20–29	49.1	33.3*	41.1	31.8**
30–39	53.9	21.2*	24.9	28.2
40–49	48.2	20.0*	9.9	10.2
50–59	41.8	22.9*	5.1	8.2***
60–69		15.5		2.6
70–79		13.0		2.0
80+		0.0		0.0
Standardized means	48.0	17.5*	17.0	13.8***

In 1984 the highest decade was 50–59 years.

p: (year 2001 vs year 1984) **p* < 0.001, ***p* < 0.01, ****p* < 0.05.

Table 3
Mean values and distribution among age-classes (males).

Age-class (years)	TC	HDL-C	LDL-C	TG	Apo A-1	Apo B	Lp(a)	G	Syst	Diast	W	H	W/H	BMI	HCY
20–29	171.4	48.6	106.7	79.5	135.7	85.5	27.5	88.0	117.2	75.7	81.2	95.8	0.85	24.1	8.33
30–39	217.3	50.2	143.7	117.8	136.0	112.8	29.8	93.4	121.0	81.4	89.5	100.2	0.89	27.0	14.38
40–49	220.0	49.9	145.3	127.7	135.6	112.6	31.8	101.3	125.4	83.7	91.6	99.6	0.92	27.3	10.78
50–59	226.7	52.4	150.7	119.2	134.8	116.9	34.4	109.9	134.0	86.7	95.4	100.7	0.95	28.4	10.93
60–69	223.3	52.4	148.8	110.1	137.8	115.9	37.1	111.3	140.8	86.8	97.9	102.5	0.96	29.2	9.92
70–79	218.1	53.7	144.2	101.2	142.4	111.6	32.1	107.9	146.0	84.9	96.7	101.5	0.95	28.4	12.62
80+	206.7	52.9	137.3	82.7	139.4	105.7	29.7	101.1	146.1	80.0	93.7	100.4	0.93	26.9	13.26
Stand. mean	208.7	50.8	137.5	107.8	136.5	107.5	31.6	100.1	128.5	82.4	90.9	99.6	0.91	27.1	11.46
S.E. of the mean	0.95	0.28	0.74	1.29	0.72	0.62	0.22	0.36	0.39	0.26	0.28	0.30	0.005	0.20	0.09

Abbreviations; (mg/dl):TC = Total cholesterol; HDL-C = HDL-cholesterol; LDL-C = LDL-cholesterol; TG = triglycerides; Apo A-1 = Apolipoprotein A-1; Apo B = Apolipoprotein B; Lp(a) = lipoprotein (a); G = plasma glucose; (mm Hg): Syst = systolic blood pressure; Diast = diastolic blood pressure; (cm):W = Waist; H = Hip; W/H = Waist/Hip ratio; (Weight/Height²): BMI = body mass index; (μmol/L): HCY = homocysteine.

the distribution by 10-year age groups of the Italian population from the 1991 census.

3. Results

The prevalence of smokers was 17.5% in males and 13.8% in females. Male smokers showed a decreasing trend from 33.3% at 20–29 decade to 0.0% at age over 80. A similar trend was present for females; from 31.8% to 0.0%. In the year 1984 (highest decade 50–59 years) the prevalence of smokers was 48.0% in males ($p < 0.001$ vs 2001) and 17.0% in females ($p < 0.05$ vs 2001) [Table 2].

From the dietary habits collected in the food frequency questionnaires, alcohol consumption (the proportion drinking up to 3 drinks daily in males and 2 drinks in females) remained stable: (80% of males; 90% of females) [26].

Tables 3 (males) and 4 (females) show a complete picture of all variables. The age-standardized mean total cholesterol level was (mg/dl) 208.7 in males and 211.1 in females, reaching 50–59 years in both sexes (226.7 and 232.6 respectively). LDL-cholesterol followed the same course (150.7 and 153.3, males and females respectively at 50–59 years). The Apolipoprotein B peak, for males and females, was 116.9 and 113.3 respectively at 50–59 years. HDL-cholesterol and Apolipoprotein A-1 were higher in females (HDL: 61.0; ApoA-1:152.5) than in males; once again the peak was at 50–59 years. Mean levels for triglycerides were in the normal range in both sexes. Lp(a) levels were higher than normal values for both sexes; 31.6 mg/dl for males and 33.7 for females. Plasma homocysteine mean levels were within normal ranges for both sexes. As far as blood pressure is concerned, the mean age-standardized systolic and diastolic pressure were in the normal range. From 60 years up, systolic pressure exceeded normal values (systolic hypertension) for both sexes. Diastolic blood pressure paralleled BMI with a peak in the middle age for both sexes. Age-standardized BMI mean levels were in the adiposity range (27.1 in males; 26.7 in females). Waist/Hip ratios were in the normal range for both sexes. In the whole sample, age-

standardized mean blood glucose levels were 100.1 in males and 95.3 in females; peaking beyond normal values were over 40 years in males and over 60 years in females.

Regarding physical activity, we recorded a general decrease during last years in walking and sport activity in the Sardinian population (data not shown).

In the population examined, 4.9% were consuming statins for hypercholesterolemia while 7.8% were taking antihypertensive drugs in monotherapy or in combination, 6.5% were receiving acetylsalicylic acid, and 2.0% were taking hypoglycemic drugs.

In Table 5 a comparison is made among RIFLE 1980, Sardinia 1999–2001 and Italy OEC 1998–2002, as far as CVD risk factors in the last twenty years are concerned. Note that age classes of Insular Italy and Italy OEC range from 35 to 64 years while those of Sardinia range from 20 to 80+ years. In both sexes, plasma total cholesterol was lower in Italy OEC and blood pressure was lower in Sardinia, while no differences were present for BMI.

In Table 6 the values refer to age classes 20–59 years from 1978 to 2001; those in 1992 and 1995 were recorded during the ATS-Sardegna Campaign for CVD prevention and Health promotion [13]. An increasing time trend existed for total cholesterol ($p < 0.05$) and HDL-cholesterol ($p < 0.01$) in both sexes, with a temporary decrease of total cholesterol at the end of the ATS-Sardegna Campaign. Regarding smokers, an opposite time trend ($p < 0.001$) was found in the two sexes, with an important decrease for males. We recorded significant differences in female BMI.

4. Discussion

The main findings of the present survey, compared with the previous surveys, were that lipid levels increased over the years, while blood pressure and smoking prevalence decreased and BMI values did not change.

Table 4
Mean values and distribution among age-classes (females).

Age-class (years)	TC	HDL-C	LDL-C	TG	Apo A-1	Apo B	Lp(a)	G	Syst	Diast	W	H	W/H	BMI	HCY
20–29	182.1	62.3	107.4	63.0	159.0	86.2	28.0	81.7	106.8	70.6	68.4	93.1	0.73	21.9	6.74
30–39	197.8	60.0	122.9	73.9	151.1	95.0	31.0	88.4	111.4	75.2	75.1	96.6	0.78	24.5	8.51
40–49	207.3	62.1	129.8	76.3	150.1	96.2	32.1	91.3	118.2	79.0	79.6	99.3	0.80	26.5	7.96
50–59	232.6	61.8	153.3	90.0	151.9	113.3	37.8	99.4	132.6	84.9	86.5	104.0	0.83	29.5	8.08
60–69	229.2	60.0	149.8	95.3	147.9	111.1	38.5	105.7	142.6	86.9	90.8	106.9	0.85	30.7	8.29
70–79	229.0	60.4	148.4	101.9	150.0	110.9	36.5	115.7	145.0	84.9	89.1	104.9	0.85	29.9	10.21
80+	227.0	57.9	149.5	98.2	159.5	115.4	37.2	102.1	146.0	80.2	87.1	101.3	0.86	27.8	15.03
Stand. mean	211.1	61.0	133.8	82.0	152.5	101.4	33.7	95.3	124.8	79.4	80.7	100.1	0.80	26.7	9.26
S.E. of the mean	0.86	0.26	0.74	0.95	0.70	0.56	0.22	0.36	0.45	0.26	0.25	0.31	0.005	0.20	0.08

Abbreviations; (mg/dl): TC = total cholesterol; HDL-C = HDL-cholesterol; LDL-C = LDL-cholesterol; TG = triglycerides; Apo A-1 = apolipoprotein A-1; Apo B = Apolipoprotein B; Lp(a) = lipoprotein (a); G = plasma glucose; (mm Hg): Syst = systolic blood pressure; Diast = diastolic blood pressure; (cm):W = Waist; H = Hip; W/H = Waist/Hip ratio; (Weight/Height²): BMI = body mass index; (μmol/L): HCY = Homocysteine.

Table 5
Comparison of some variables among RIFLE 1980 (South and Islands) [12], Sardinia 1999–2001 (present survey), and Italy OEC 1998–2002 [14].

	Men			Women		
	RIFLE 1980	Sardinia 1999–2001	Italy OEC 1998–2002	RIFLE 1980	Sardinia 1999–2001	Italy OEC 1998–2002
TC	208	209	205***	208	211	204**
HDL-C	46	51***	49	52	61**	59
TG	140	138		111	134**	
Syst	135	129**	133***	137	125*	128***
Diast	86	82*	86*	86	79*	81*
BMI	27	27	27	28	27	26

* $p < 0.001$; ** $p < 0.01$; *** $p < 0.05$, vs the column on the left.

Abbreviations; (mg/dl): TC = total cholesterol; HDL-C = HDL-cholesterol; LDL-C = LDL-cholesterol; TG = triglycerides; (mm Hg): Syst = systolic blood pressure; Diast = diastolic blood pressure; BMI = body mass index; (Weight/Height²).

Prevalence of current smokers was lower than in past surveys (as shown in Table 6) even in females, in spite of their still high prevalence in the age-range 30–39, in which they exceed males (28.2% vs 21.2% in Table 2). The comparison of smoking habits recorded in 1984 [24] and in 2001 in the four decades 20–59 years showed a significant decrease in each decade of males, while this was present for females only in the 20–29 year decade; on the contrary, in 2001 an increase in smoking habits was found in females 50–59 years (Table 2). The global fall in percent of smokers of both sexes took place after the ATS-Sardegna Campaign [13]. Similarly to the WHO MONICA Project [7], decrease of smoking was more evident in women with higher smoking habit. Note that in both males and females aged 20–59 years the decrease in smoking habit from 1978 to 2001 paralleled that reported for the whole Italy [25].

The consumption of alcohol in Sardinia paralleled that of the mean of whole Italy. It was mainly wine consumption during meals [26].

Plasma lipid profile was just above the optimal values recommended by ATP III [19]; in particular, LDL-C was borderline high (between 130 and 159 mg/dl) in both sexes (Tables 3 and 4). Compared with the mainland (Table 5), values were slightly higher, but sharply lower than those recorded by the RIFLE survey two decades ago [12]. This was true for 1980s Italy but not for 1980s Sardinia. The higher levels of HDL-C and Apo A-1 in females than in males are paralleled by lower TG values except for the elderly, indicating the well known opposite behaviour between the two circulating lipoproteins [27]. Trends in lipid profile in Sardinia from 1978 to 2001 (Table 6) showed a steady increase, interrupted between 1992 and 1995 during the ATS-Sardegna Campaign [13] and resumed after its termination, as the present data demonstrated.

Lp(a) levels were high in both sexes, exceeding the normal values of 30 mg/dl not only in age classes from 40–49 on, but also in age-standardized overall means, in both sexes (Tables 3 and 4) [28]. Considerable ethnic variation of plasma Lp(a) concentrations has been previously associated with Apo[a] phenotype, with Ghanaians showing almost 2-fold mean plasma values (36.2 mg/dl) than Germans (18.7 mg/dl) [29]. Sardinians are an ancient population of pre-Neolithic origin, so that they may have undergone considerable genetic drift and are therefore different from other European populations, showing instead a genetic resemblance to the Lebanese population [30], whose Lp(a) levels are rather high [31].

Plasma glucose levels partially increased with age, as shown in 50–79 males (Table 3) and in 60–79 year old females (Table 4).

As expected, blood pressure values increased with age; until 59 years, age-standardized values of systolic and diastolic blood pressure in both sexes (Tables 3 and 4) were lower than the prehypertensive status as defined by Chobanian et al. [17]. Compared with other Italian areas, they were likewise lower (Table 5). As for other CVD risk factors, blood pressure values decreased during the

ATS-Sardegna Campaign in both sexes (Table 6) very likely because of reduced salt consumption [13].

Waist circumference and waist to hip ratio, that are measures of abdominal obesity [32] were below ATP III limits for identifying the metabolic syndrome (WC 102 cm in men and 88 cm in women) [19], with a lower CHD risk, as far as the metabolic syndrome is concerned.

Plasma homocysteine levels were within the normal range in both sexes but with a graded risk in several aged classes (Tables 3 and 4), with values ranging from 10 to 15 $\mu\text{mol/L}$ [23].

Overall, Sardinians showed a peculiar increased plasma Lp(a) levels in both sexes when compared with continental Italians [33] increasing thus CHD risk [16], while waist circumference pointed to the contrary. CVD are a typical example of gene–environment interaction; since we found important changes in risk factors in short period of time, the responsibility of environment seems to be predominant.

In spite of the increasing levels of several risk factors for CVD in Sardinia, mortality from CVD [34] remained low. This was probably ascribable to two main reasons. One is the still followed Mediterranean diet [35], which is very effective in preventing CHD [36]. Another is the high prevalence in Sardinia of glucose-6-phosphate dehydrogenase deficiency, which resulted protective against CVD [37].

Some limitations of the present study must be acknowledged. The participation rate to the survey (69.48%) can not be considered high; however, given the particular homogeneity of Sardinian population [24], this rate can be considered representative for the island. As in many other epidemiological surveys, the biophysical and biochemical parameters have been measured only once: this may prevent us from considering absolutely valid the results. Moreover, a comparison between about 70% of participants and 30% of those refusing participation was not performed.

In conclusion, in the Sardinian population several emerging risk factors were present. It is interesting to note that in the last years CVD risk factors increased in the general population, with the only exception during the ATS-Sardegna Campaign period, in which a favourable trend was obtained for most of them [13]. The fact that risk factors resumed their increase after the cessation of the Campaign demonstrates that the messages have to be renewed for a longer period through the population strategy, whose power can obtain great results with a relatively low economic cost [38].

Table 6
Comparison of some variables in the Sardinian population from 1978 to 2001.

	1978	1984	1992	1995	2001	p for trend
MALES						
TC	189	206*	215*	209***	216***	<0.05
HDL-C		46	48	47	50**	<0.01
LDL-C		136	143*	138**	144***	<0.05
TG	124	118	122	120	114	
Syst	125	130	129	125***	126	
Diast	86	81*	83**	80***	81	
BMI	25	25	26	26	27	
Smokers	58	49**	43***	41	24*	<0.001
FEMALES						
TC	184	197*	212*	210	217**	<0.05
HDL-C		50	54**	55	65**	<0.01
LDL-C		127	139*	136***	135	<0.05
TG	92	94	96	96	85	
Syst	125	129*	128	124***	119*	
Diast	86	81**	85*	82***	78**	
BMI	27	25**	26***	26	26	
Smokers	14	22**	28***	31	20*	<0.001

Between | the values recorded during the ATS-SARDEGNA Campaign for CVD prevention and Health promotion (1992–1995). * $p < 0.001$; ** $p < 0.01$; *** $p < 0.05$, vs the column on the left. Abbreviations; (mg/dl): TC = total cholesterol; HDL-C = HDL-cholesterol; LDL-C = LDL-cholesterol; TG = triglycerides; (mm Hg): Syst = systolic blood pressure; Diast = diastolic blood pressure; BMI = body mass index (Weight/Height²); Smokers: prevalence (%).

5. Learning points

- Important changes in lifestyle are influencing risk factor levels in Sardinia.
- In the last years CVD risk factors increased in the general population, with the only exception during the ATS-SARDEGNA Campaign period, in which a favourable trend was obtained for most of them. This demonstrates that the Campaign has been terminated too early.
- A peculiar increase in plasma Lp(a) levels in the Sardinian population was present for both sexes when compared with Italians from other regions. This confirms, in our opinion, the genetic differences between Sardinians and other European populations, including continental Italians.

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