

Original article

# Cardiovascular Risk Factors in Spain in the First Decade of the 21st Century, a Pooled Analysis With Individual Data From 11 Population-Based Studies: the DARIOS Study<sup>☆</sup>

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## ABSTRACT

**Introduction and objectives:** To estimate the prevalence of cardiovascular risk factors in individuals aged 35-74 years in 10 of Spain's autonomous communities and determine the geographic variation of cardiovascular risk factors distribution.

**Methods:** Pooled analysis with individual data from 11 studies conducted in the first decade of the 21st century. The average response rate was 73%. Lipid profile (with laboratory cross-validation), glucose level, blood pressure, waist circumference, height, and weight were measured and standard questionnaires administered. Age-standardized prevalence of smoking, diabetes, hypertension, dyslipidemia, and obesity in the European population were calculated. Furthermore, the coefficient of variation between component studies was determined for the prevalence of each risk factor.

**Results:** In total, 28,887 participants were included. The most prevalent cardiovascular risk factors were high blood pressure (47% in men, 39% in women), total cholesterol  $\geq 250$  mg/dL (43% and 40%, respectively), obesity (29% and 29%, respectively), tobacco use (33% and 21%, respectively), and diabetes (16% and 11%, respectively). Total cholesterol  $\geq 190$  and  $\geq 250$  mg/dL were the respective minimum and maximum coefficients of variation (7%-24% in men, 7%-26% in women). Average concordance in lipid measurements between laboratories was excellent.

**Conclusions:** Prevalence of high blood pressure, dyslipidemia, obesity, tobacco use and diabetes is high. Little variation was observed between autonomous communities in the population aged 35-74 years. However, presence of the most prevalent cardiovascular risk factors in the Canary Islands, Extremadura and Andalusia was greater than the mean of the 11 studies.

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## Factores de riesgo cardiovascular en España en la primera década del siglo XXI: análisis agrupado con datos individuales de 11 estudios de base poblacional, estudio DARIOS

### RESUMEN

#### Palabras clave:

Enfermedades cardiovasculares  
Factores de riesgo  
Lípidos  
Mortalidad  
Presión arterial  
Diabetes mellitus  
Obesidad  
Tabaquismo  
Epidemiología  
Prevalencia

**Introducción y objetivos:** Analizar la prevalencia de factores de riesgo cardiovascular en personas de 35-74 años en 10 comunidades autónomas españolas y determinar el grado de variabilidad geográfica en la distribución de los factores de riesgo cardiovascular.

**Métodos:** Análisis agrupado con datos individuales de 11 estudios desarrollados en la primera década del siglo XXI con un promedio de tasa de participación del 73%. Se midió el perfil lipídico (con validación cruzada de laboratorios), glucemia, presión arterial, perímetro de la cintura, peso y talla y se administraron cuestionarios estandarizados. Se estimó la prevalencia estandarizada a la población europea de tabaquismo, diabetes, hipertensión arterial, dislipemia y obesidad. Además, se estimó el coeficiente de variación entre estudios componentes en la prevalencia de cada factor de riesgo.

**Resultados:** Se incluyó a 28.887 participantes. Los factores de riesgo cardiovascular más prevalentes fueron: hipertensión arterial (el 47% en varones y el 39% en mujeres), dislipemia con colesterol total  $\geq 250$  mg/dl (el 43 y el 40%), obesidad (el 29% en ambos sexos), tabaquismo (el 33 y el 21%) y diabetes mellitus (el 16 y el 11%). El colesterol total  $\geq 190$  y  $\geq 250$  mg/dl presentó el coeficiente de variación mínimo y máximo, respectivamente (el 7-24% en varones y el 7-26% en mujeres). La concordancia media en las determinaciones lipídicas entre laboratorios fue excelente.

**Conclusiones:** La prevalencia de hipertensión arterial, dislipemia, obesidad, tabaquismo y diabetes mellitus, es elevada, con variabilidad relativamente baja en la población de 35 a 74 años entre comunidades autónomas. Canarias, Extremadura y Andalucía presentan mayor número de factores de riesgo cardiovascular significativamente más prevalentes que el promedio de los 11 estudios componentes.

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### Abbreviations

BMI: body mass index  
CV: coefficient of variation  
HBP: high blood pressure  
HDLc: high-density lipoprotein cholesterol  
LDLc: low-density lipoprotein cholesterol  
NHS: National Health Survey

### INTRODUCTION

Cardiovascular disease is the primary cause of death in the Spanish population.<sup>1</sup> The detection and control of cardiovascular risk factors remains the essential preventive strategy.<sup>2</sup> In Spain, data from population-based studies on cholesterol trends in the past decade are inconclusive. Some studies show a fall in cholesterol,<sup>3</sup> whereas other authors indicate an increase.<sup>4</sup> Furthermore, improved control of high blood pressure (HPB) has been observed,<sup>3</sup> in contrast with the increased prevalence of obesity,<sup>5</sup> diabetes mellitus,<sup>6</sup> and tobacco use, particularly in women.<sup>3</sup>

The absence of objective measures in Spain's National Health Survey (NHS)<sup>7</sup> prevents us from determining the real countrywide prevalence of cardiovascular risk factors. However, population-based epidemiologic studies including anthropometric measures, blood pressure data and laboratory tests do enable us to accurately determine prevalence in representative samples.

Earlier studies indicated substantial variability in cardiovascular risk factors prevalence between autonomous communities.<sup>8,9</sup> The epidemiologic wing of the present study (DARIOS-Epidemiológico) examines dyslipidemia, atherosclerotic risk, increased high-sensitivity C-reactive protein (hsCRP), and inflammatory and oxidative status in the Spanish population. It is a pooled analysis with individual data from studies using comparable methods that have been conducted in Spain in the population aged 35-74 since 2000.

The objective is to analyze combined cardiovascular risk factors prevalence in 11 studies conducted in 10 of Spain's autonomous communities in the first decade of the 21st century and determine the level of geographic variability of cardiovascular risk factors distribution.

### METHODS

#### Study Population

Pooled analysis with individual data from 11 population-based studies conducted in different geographical areas of Spain (in parentheses) since 2000 with similar methodological designs: ARTPER<sup>10</sup> (Catalonia-Barcelona), CDC de Canarias<sup>11</sup> (the Canary Islands), CORSAIB<sup>12</sup> (Balearic Islands), DINO<sup>13</sup> (Region of Murcia), DRECA-2<sup>14</sup> (Andalusia), HERMEX<sup>15</sup> (Extremadura), PREDIMERC<sup>16</sup> (Community of Madrid), RECCYL<sup>17</sup> (Castile and Leon), REGICOR<sup>3</sup> (Catalonia-Girona), RIVANA<sup>18</sup> (Community of Navarra) and TALAVERA<sup>19</sup> (Castile-La Mancha) (Table 1). These studies included patients aged 35-74 years, except ARTPER, which enrolled participants in the 49-74 age range.<sup>10</sup> All participants gave written informed consent to take part in the component studies. The DARIOS study was approved by the Municipal Healthcare Institute's Clinical Research Ethics Committee (authorization n° 2009/3640).

#### Measurements

##### Questionnaires and Physical Examination

The component studies' questionnaires were based on standardized World Health Organization (WHO) surveys.<sup>20</sup> Socio-demographic variables and data on tobacco use and history of HBP, dyslipidemia, and diabetes were recorded. Prevalence of current smokers, ex-smokers (>1 year), and non-smokers was calculated.

Trained healthcare workers conducted the physical examinations. The participants' waist circumference, weight, and height were measured. Body mass index (BMI) was calculated, dividing

**Table 1**  
General Characteristics of the DARIOS Study and Each Components Study

	ARTPER <sup>10</sup> (45-74 years)	CDC <sup>11</sup>	CORSAIB <sup>12</sup>	DINO <sup>13</sup>	DRECA-2 <sup>14</sup>	HERMEX <sup>15</sup>	PREDIMERC <sup>16</sup>	RECCyL <sup>17</sup>	REGICOR <sup>3</sup>	RIVANA <sup>18</sup>	TALAVERA <sup>19</sup>	General
Participants, n (%)	3232 (11)	4715 (16)	1669 (6)	945 (3)	1599 (6)	2204 (8)	2003 (7)	2436 (8)	5694 (20)	3862 (13)	528 (2)	28 887 (100)
Age (years), mean ± SD	62 ± 7	49 ± 9	54 ± 11	53 ± 12	53 ± 11	52 ± 11	53 ± 12	54 ± 12	54 ± 11	52 ± 11	57 ± 12	54 ± 11
Men, %	46	44	48	47	46	48	48	50	47	46	46	46
Age groups												
35-44, n (%)	—	1772 (38)	442 (26)	304 (32)	489 (31)	671 (30)	684 (34)	698 (29)	1346 (24)	1193 (31)	104 (20)	7703 (27)
45-54, n (%)	572 (18)	1424 (30)	442 (26)	239 (25)	422 (26)	615 (28)	444 (22)	554 (23)	1566 (28)	1124 (29)	123 (23)	7525 (26)
55-64, n (%)	1476 (46)	1347 (29)	425 (25)	200 (21)	380 (24)	502 (23)	443 (22)	585 (24)	1514 (27)	880 (23)	121 (23)	7873 (27)
65-74, n (%)	1184 (37)	172 (4)	360 (22)	202 (21)	308 (19)	416 (19)	432 (22)	599 (25)	1268 (22)	665 (17)	180 (34)	5786 (20)
Geographical area	Two districts in Barcelona province	Autonomous Community of the Canary Islands	Autonomous Community of the Balearic Islands	Region of Murcia	Autonomous Community of Andalusia	HCA D. Benito-Villanueva de la Serena (Badajoz)	Autonomous Community of Madrid	Autonomous Community of Castile and Leon	6 districts in Girona province	Community of Navarra	HCA Talavera de la Reina (Toledo)	—
Reference population (35-74)	178 624	1 055 370	340 675	516 609	3 695 353	54 098	3 129 232	1 201 873	290 336	268 470	29 773	10 760 413
Response rate, %	63	70	77	63	95	81	58	81	72	74	75	73
Sample type	Random	Random	Random	Random	Random	Random	Random	Random	Random	Random	Random	—
Context of sampling	Healthcare ID card census	Population census	Healthcare ID card census	Healthcare ID card census	Population census	Healthcare ID card census	Healthcare ID card census	Healthcare ID card census	Population census	Population census	Municipal census	—
Enrollment period	2006-2008	2000-2005	2000	2001-2003	2006-2007	2008-2009	2007	2004	2004-2006	2004-2005	2006	—

HCA, health care area; ID, identity; SD, standard deviation.

weight by height squared (kg/m<sup>2</sup>) to define the categories of overweight and obesity as in the Spanish Society for the Study of Obesity classification.<sup>21</sup> Adult Treatment Panel III cutoff points for waist circumference (>102 cm in men, > 88 cm in women) were used.<sup>22</sup>

Prevalence of HBP was estimated using the lower of the first 2 blood pressure measurements, in line with 7th Joint National Committee Report cutoff points.<sup>23</sup> The following definitions were established: a) diagnosed HBP: participants diagnosed by a standardized questionnaire, and b) real HBP: participants diagnosed or presenting with systolic blood pressure  $\geq$ 140 mmHg or diastolic blood pressure  $\geq$ 90 mmHg.<sup>23</sup>

#### Laboratory Measurements

Blood samples were taken following a > 10 h fast. Analysis was performed in local laboratories on fresh blood or aliquots of serum stored at -80 °C in samples not previously thawed. Triglycerides, glucose, and total cholesterol were measured using enzymatic methods. All local laboratories satisfied external quality-control requirements.<sup>3,10-19</sup> When triglycerides were < 300 mg/dL, low density lipoprotein cholesterol (LDLc) was calculated using the Friedewald formula, to avoid underestimating LDLc.

A concordance study of the CDC-Canarias, CORSAIB, DRECA-2, HERMEX, PREDIMERC, RECCyL, and RIVANA laboratories (64% of the sample) was conducted. From each study, 100 samples were analyzed for total cholesterol, high density lipoprotein cholesterol (HDLc), and triglycerides using the IMIM laboratory—originally used by REGICOR and TALAVERA (22% of the sample)—as reference. The IMIM laboratory used esterase-oxidase-peroxidase (CHOD-PAP, ABX-Horiba, Montpellier, France) to measure cholesterol. Triglycerides were measured with glycerol-phosphate oxidase-peroxidase (GPO-PAP, ABX-Horiba). Direct HDLc measurement was with selective accelerator detergent (ABX-Horiba). The ARTPER and DINO studies (14% of the sample) were unable to provide samples for the concordance study.

Prevalence was calculated for: a) diagnosed diabetes mellitus (participants diagnosed by a standardized questionnaire); b) real diabetes mellitus (participants diagnosed or with glucose level  $\geq$ 126 mg/dL), and c) impaired fasting glucose (participants not diagnosed with diabetes mellitus and with glucose level 110-125 mg/dL).<sup>24</sup>

Prevalence was calculated for: a) diagnosed dyslipidemia (participants diagnosed by a standardized questionnaire), and b) real dyslipidemia (participants diagnosed or presenting total cholesterol  $\geq$ 190,  $\geq$ 240 or  $\geq$ 250 mg/dL or LDLc  $\geq$ 115 or  $\geq$ 160 mg/dL, depending on clinical practice guidelines).<sup>24-26</sup> Prevalence of hypoalphalipoproteinemia was determined (LDLc < 40 in men and < 50 mg/dL in women).

#### Statistical Analysis

Age-standardized prevalence was determined for each RF in each component study. To do this, individuals were categorized in 5-year age groups and a rough prevalence figure calculated. This was later standardized by the direct method, with reference to the European population.<sup>27</sup> These figures were accompanied by the 95% confidence interval for the cardiovascular risk factors, stratified by sex for each component study and for the combined studies. Heterogeneity between individual studies was determined with the Levene test for homogeneity of variances between all participating centers for the principle variables. Individuals were classified in 8 groups by age and sex. To calculate the mean or general prevalence of each cardiovascular risk factors and the corresponding confidence intervals, we combined the estimates

obtained individually for each study using the DerSimonian-Laird random-effects method to compensate for differences in sample size. Prevalences were compared by age group with NHS results for 2006. Continuous variables are described as mean and 95% confidence interval, also standardized for the European population. The standardized ratio of prevalences was calculated, centering the mean of all component studies to 100% and calculating deviations from this point for each component study and risk factor: tobacco use, systolic blood pressure  $\geq 140$  mmHg or diastolic blood pressure  $\geq 90$  mmHg, total cholesterol  $\geq 250$  and  $\geq 190$  mg/dL, BMI  $\geq 30$ , and glucose level  $\geq 126$  mg/dL.

The coefficient of variation (CV) was estimated to determine variability between component studies in the prevalence of each risk factor, calculating the percentage deviation of each study versus the average of all studies using the following formula:

$$CV = (\text{standard deviation of prevalences} / \text{mean of prevalences}) \times 100$$

This CV corresponded to the standard deviation of the 11 studies. Pearson's correlation coefficients were calculated to analyze deviations in each study with respect to mortality from ischemic heart disease for 2007, standardized for the European population, in each autonomous community.<sup>28</sup> Data from ARTPER were excluded because of differences in the age distribution (individuals aged > 49 years) with respect to the other studies.

Concordance of lipid measurements with the reference laboratory was measured using the coefficient of determination R<sup>2</sup>, intraclass correlation coefficient, and Bland-Altman graphics that analyze the relation between mean values of the original measurement and the reference mean, and the differences between the two.<sup>29</sup> The effect of outliers was analyzed through a graphic representation of residuals. Points that differed by > 40 mg/dL for total cholesterol, > 10 mg/dL for HDLc, and > 40 mg/dL for triglycerides, between the original measurement and that of the reference laboratory were considered sampling errors and eliminated; the graphics were redrawn. When 95% of differences were within  $\pm 5\%$  of the reference laboratory mean determination, participating center and reference laboratory results were considered equivalent. When the value range was outside of  $\pm 5\%$ , the Deming regression was used to correct the original values<sup>30</sup> if systematic bias was observed in the figures.

Statistical Analysis was conducted with R Version 2.10 (R Foundation for Statistical Computing, Vienna, Austria).

## RESULTS

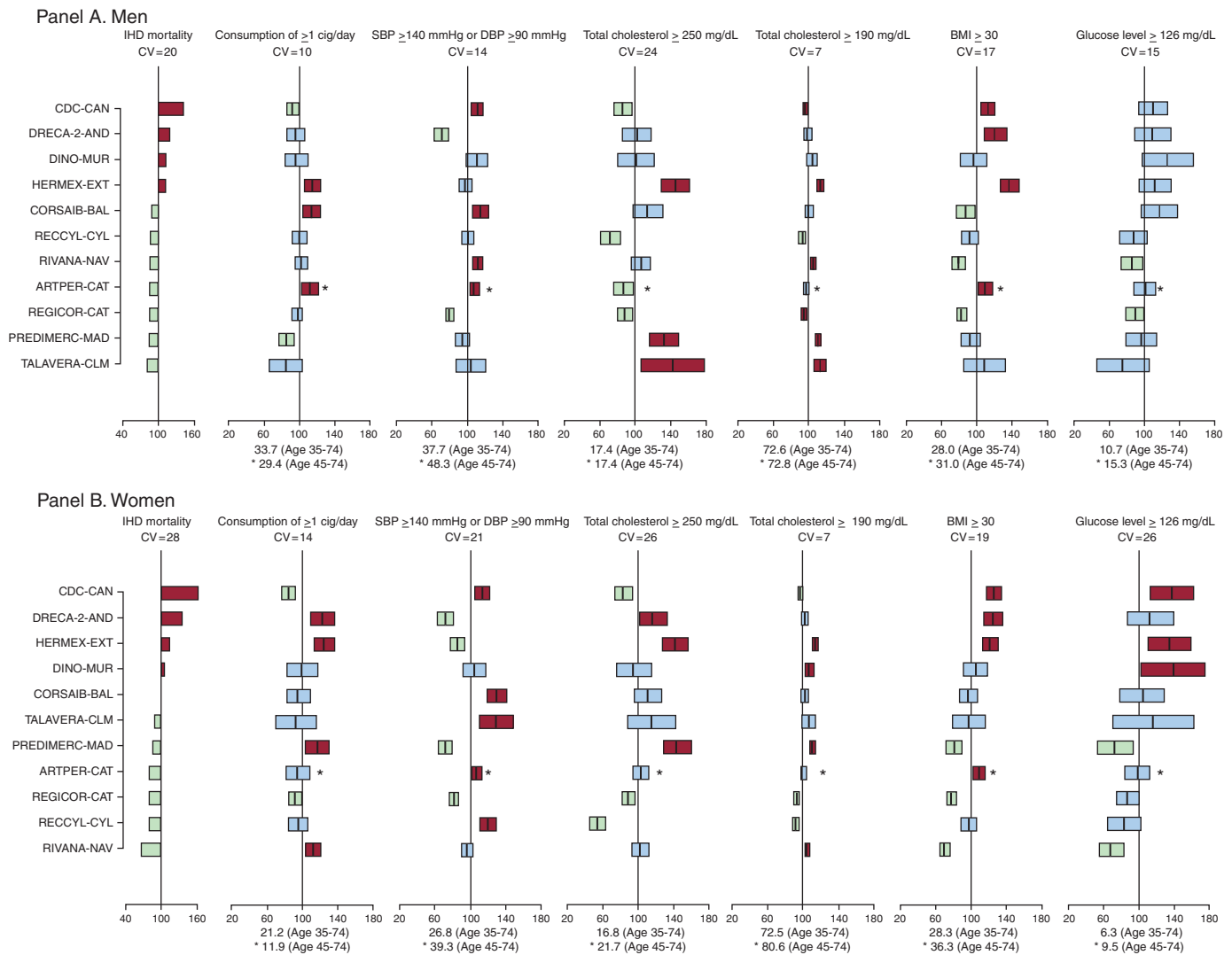
The study enrolled 28 887 participants from the following 10 autonomous communities: Andalusia, Balearic Islands, Canary Islands, Castile-La Mancha, Castile and Leon, Catalonia, Extremadura, Community of Madrid, Region of Murcia and Community of Navarra. Their total population represents approximately 70% of the Spanish population aged 35-74. Table 1 presents the characteristics of each component study. Significant heterogeneity ( $P < .05$ ) was found for systolic blood pressure in all age groups of women, whereas in men it was found in all age groups except the 55-64 year range. Significant heterogeneity was found for diastolic blood pressure in men aged < 45 years and in all age groups in women. For total cholesterol, we found heterogeneity only in women aged > 45 years.

Table 2 presents values of glucose level, blood pressure and prevalences of impaired fasting glucose, diabetes mellitus and diagnosed and real HBP by sex. Independently of the diagnosis of diabetes mellitus, women in the CDC, DINO and HERMEX studies presented a prevalence of baseline glucose level  $\geq 126$  mg/dL significantly greater than the mean (Fig. 1). Similarly, independently of the diagnosis of HBP, prevalence of systolic blood

**Table 2** Glucose Level, Systolic Blood Pressure and Diastolic Blood Pressure and Prevalence of Diabetes and High Blood Pressure Standardized to the European Population by Component Study and General Study in Men and Women Aged 35-74 Years

	ARTPER (45-74 years)	CDC	CORSAIB	DINO	DRECA-2	HERMEX	PREDIMERC	RECCYL	REGICOR	RIVANA	TALAVERA	General
Men, n	1493	2054	804	443	736	1046	966	1198	2685	1765	235	13 425
Glucose level, mg/dL	110 (108-112)	105 (104-106)	106 (104-109)	105 (102-108)	100 (97-103)	109 (107-110)	104 (102-106)	102 (101-104)	102 (101-103)	106 (104-107)	103 (100-106)	105 (103-106)
IFG, %	13 (11-15)	12 (10-14)	12 (9-14)	11 (8-14)	5 (4-7)	20 (18-23)	11 (8-13)	12 (10-14)	9 (8-10)	17 (15-18)	11 (6-16)	12 (10-14)
Diagnosed DM, %	25 (22-27)	13 (12-15)	12 (10-14)	14 (10-17)	14 (12-16)	11 (9-13)	10 (8-11)	7 (6-9)	12 (11-14)	10 (9-11)	13 (8-17)	13 (10-15)
Real DM, %	27 (25-30)	17 (15-19)	17 (14-19)	16 (12-19)	17 (15-20)	16 (14-18)	13 (11-15)	11 (10-13)	15 (14-16)	13 (11-14)	15 (10-20)	16 (14-18)
SBP, mmHg	137 (136-138)	128 (127-129)	131 (130-133)	132 (131-134)	124 (123-125)	130 (129-131)	131 (130-132)	130 (129-131)	127 (126-127)	133 (132-134)	132 (130-134)	131 (128-133)
DBP, mmHg	79 (79-80)	80 (80-81)	81 (81-82)	81 (80-82)	75 (74-76)	76 (75-77)	80 (79-81)	79 (79-80)	80 (79-80)	80 (79-80)	80 (79-82)	79 (78-80)
Diagnosed HBP, %	44 (42-47)	31 (29-33)	27 (24-29)	25 (21-29)	30 (27-33)	30 (27-33)	35 (32-38)	19 (17-22)	31 (29-33)	27 (25-29)	23 (18-28)	29 (26-33)
Real HBP, %	64 (61-66)	50 (47-52)	46 (42-49)	46 (42-51)	42 (39-45)	43 (40-45)	47 (44-50)	44 (41-46)	41 (39-43)	45 (43-48)	44 (38-50)	47 (42-51)
Women, n	1739	2661	865	502	863	1158	1037	1238	3009	2097	293	15 462
Glucose level, mg/dL	102 (101-103)	100 (98-101)	99 (97-101)	96 (94-99)	91 (89-93)	101 (100-103)	96 (95-97)	96 (94-97)	94 (93-94)	97 (96-98)	97 (94-101)	97 (95-99)
IFG, %	7 (5-8)	6 (5-8)	8 (6-9)	5 (3-7)	4 (2-5)	9 (7-11)	6 (5-8)	6 (5-8)	4 (4-5)	6 (5-7)	3 (1-5)	6 (5-7)
Diagnosed DM, %	16 (14-18)	13 (12-15)	10 (8-12)	11 (8-14)	11 (9-13)	10 (9-12)	6 (5-7)	5 (4-6)	8 (7-9)	7 (6-8)	8 (5-10)	10 (8-11)
Real DM, %	18 (16-20)	14 (13-16)	11 (9-12)	11 (8-13)	13 (11-15)	13 (11-15)	7 (5-8)	7 (6-8)	10 (9-11)	8 (7-10)	10 (7-13)	11 (9-13)
SBP, mmHg	133 (132-133)	123 (122-124)	126 (125-127)	121 (119-122)	118 (117-119)	119 (118-120)	121 (120-122)	127 (126-128)	120 (120-121)	123 (123-124)	126 (124-129)	122 (121-126)
DBP, mmHg	78 (77-78)	76 (76-76)	79 (78-79)	74 (73-75)	71 (70-72)	71 (71-72)	74 (74-75)	77 (77-78)	76 (76-76)	76 (76-77)	78 (77-79)	75 (74-77)
Diagnosed HBP, %	45 (42-47)	32 (30-34)	25 (23-28)	27 (23-30)	29 (27-32)	28 (26-30)	33 (30-36)	22 (20-24)	27 (25-28)	22 (20-24)	25 (21-30)	29 (25-33)
Real HBP, %	57 (55-60)	42 (40-44)	39 (36-41)	36 (32-40)	35 (33-38)	34 (32-36)	38 (35-41)	39 (36-41)	32 (31-34)	32 (30-34)	40 (34-45)	39 (34-43)

DBP, diastolic blood pressure; DM, diabetes mellitus; HBP, high blood pressure; IFG, impaired fasting glucose, baseline glucose level in participants without diagnosed DM 100-125 mg/dL; Real DM, diagnosed DM + glucose level  $\geq 126$  mg/dL; Real HBP, diagnosed HBP + SBP/DBP  $\geq 140/90$  mmHg; SBP, systolic blood pressure. Values are expressed as mean (95% confidence interval).



**Figure 1.** Death from ischemic heart disease, standardized for the European population by autonomous community, and standardized ratio of prevalence (mean percentage deviation with 95% confidence interval of percentage deviations) for tobacco use of  $\geq 1$  cigarettes/day, systolic blood pressure  $\geq 140$  mmHg or diastolic blood pressure  $\geq 90$  mmHg, total cholesterol  $\geq 250$  mg/dL and  $\geq 190$  mg/dL, body mass index  $\geq 30$ , baseline glucose level  $\geq 126$  mg/dL. The component studies compare each risk factor with global prevalence in the DARIOS study (100% indicated by the vertical line) in rank order of population-wide cardiovascular mortality. At the foot of each factor appears mean prevalence of the corresponding factor for the 2 age groups (35-74 years and 45-74 years). BMI, body mass index; Cig, cigarette; CV, coefficient of variation; DBP, diastolic blood pressure; IHD, ischemic heart disease; SBP, systolic blood pressure.

pressure  $\geq 140$  mmHg or diastolic blood pressure  $\geq 90$  mmHg was significantly greater than the mean in the ARTPER, CDC and CORSAIB studies in both men and women; in men, in the RIVANA study; and in women, in the RECCYL and TALAVERA studies (Fig. 1).

Prevalence of obesity, overweight, high waist circumference, and tobacco use is shown in Table 3. The ARTPER, CDC, DRECA-2 and HERMEX studies presented significantly greater prevalence of obesity than the mean in men and women (Fig. 1). Tobacco use presented little variability between studies, particularly in men. Even so, men in the ARTPER, CORSAIB and HERMEX studies and women in the DRECA-2, HERMEX, PREDIMERC, and RIVANA studies were significantly more often smokers than the mean (Table 3 and Fig. 1).

Analysis of concordance of lipid measurements showed limits of concordance of the 95%, coefficient of determination  $R^2$ , and intraclass correlation coefficient between  $\pm 14$  and  $\pm 33$ ; 0.82 and 0.97, and 0.91 and 0.98, respectively, for total cholesterol, between  $\pm 5$  and  $\pm 8$ ; 0.84 and 0.94, and 0.92 and 0.97 for HDLc,

and between  $\pm 10$  and  $\pm 25$ ; 0.94 and 0.99, and 0.97 and 0.99 for triglycerides.

Prevalence of real dyslipidemia varied notably between total cholesterol or LDLc and the chosen cutoff point (Table 4). Fig. 2 shows the distribution of total cholesterol and its fractions in men and women. Prevalence of dyslipidemia (total cholesterol  $\geq 250$  mg/dL) was significantly greater than the mean in men in the HERMEX, PREDIMERC, and PREDIMERC studies, and in women in the DRECA-2, HERMEX, and TALAVERA studies (Fig. 1). With the  $\geq 190$  mg/dL total cholesterol cutoff, variability between studies fell considerably. Even so, men and women in the HERMEX, PREDIMERC, and RIVANA studies; men in the TALAVERA study, and women in the DINO study presented prevalences significantly greater than the mean for DARIOS.

Prevalence of cardiovascular risk factors in the population aged 35-74 years was similar in the component studies (coefficient of variation 7%-24% in men and 7%-26% in women) (Fig. 1).

In women, prevalence of obesity and glucose level  $\geq 126$  mg/dL correlated significantly with death from ischemic heart disease in

**Table 3** Body Mass Index, Waist Circumference, and Prevalence of Obesity and Tobacco Use Standardized to the European Population by Component Study and General Study in Men and Women Aged 35-74 Years

	ARTIPER (45-74 years)	CDC	CORSAIB	DINO	DRECA-2	HERMEX	PREDIMERC	RECCYL	REGICOR	RIVANA	TALAVERA	General
<b>Men (n)</b>	1493	2054	804	443	736	1046	966	1198	2685	1765	235	13 425
BMI	29 (28-29)	28 (28-28)	28 (27-28)	28 (28-28)	29 (28-29)	29 (29-30)	28 (28-28)	28 (28-28)	28 (27-28)	28 (27-28)	28 (28-29)	28 (28-28)
BMI 25-29.9, %	49 (46-52)	48 (45-50)	48 (45-52)	56 (51-61)	50 (46-53)	47 (44-50)	52 (49-55)	50 (47-53)	53 (51-55)	55 (52-57)	50 (43-57)	51 (49-52)
BMI ≥30, %	34 (32-37)	32 (29-34)	25 (22-28)	27 (23-31)	34 (31-37)	38 (35-41)	26 (23-29)	26 (23-29)	23 (22-25)	22 (20-24)	30 (24-37)	29 (26-32)
WC	101 (100-102)	98 (98-99)	97 (96-98)	100 (99-101)	101 (100-102)	101 (100-101)	96 (95-96)	96 (96-97)	96 (95-97)	98 (97-98)	100 (98-102)	99 (97-100)
WC > 102 cm, %	42 (40-45)	34 (31-36)	29 (26-32)	39 (34-43)	42 (38-45)	39 (36-42)	25 (22-28)	27 (24-30)	27 (24-30)	30 (28-32)	39 (33-46)	34 (30-38)
Smoker, %	33 (30-36)	31 (29-33)	39 (35-42)	33 (28-37)	32 (29-36)	39 (36-42)	29 (26-32)	34 (31-37)	33 (31-35)	35 (32-37)	29 (22-35)	33 (32-35)
Non-smoker, %	22 (19-24)	34 (31-36)	21 (19-24)	50 (45-54)	34 (31-37)	28 (25-30)	33 (30-36)	32 (29-34)	30 (28-31)	38 (36-40)	31 (25-38)	32 (28-36)
Ex-smoker, %	45 (43-48)	35 (33-38)	40 (36-43)	17 (14-22) <sup>a</sup>	34 (30-37)	33 (31-36)	38 (35-41)	34 (32-37)	37 (36-39)	27 (25-29)	40 (34-47)	36 (33-40)
<b>Women (n)</b>	1739	2661	865	502	863	1158	1037	1238	3009	2097	293	15 462
BMI	29 (29-30)	29 (28-29)	27 (27-28)	28 (28-28)	29 (28-29)	28 (28-29)	27 (27-27)	27 (27-28)	27 (26-27)	26 (26-26)	28 (27-29)	28 (27-28)
BMI 25-29.9, %	41 (39-44)	38 (36-40)	33 (30-36)	41 (37-46)	37 (34-40)	35 (32-38)	37 (34-40)	35 (32-38)	33 (31-35)	33 (31-35)	41 (35-47)	36 (34-38)
BMI ≥30, %	40 (37-42)	36 (33-38)	27 (25-30)	30 (26-34)	35 (32-38)	35 (32-37)	23 (21-26)	28 (25-30)	22 (21-24)	20 (18-22)	28 (22-33)	29 (25-34)
WC	95 (94-95)	91 (90-91)	87 (86-87)	91 (90-91)	96 (95-96)	96 (95-96)	83 (83-84)	91 (91-92)	88 (87-89)	88 (87-88)	94 (93-96)	91 (88-93)
WC > 88 cm	68 (65-70)	56 (54-58)	41 (38-44)	56 (52-60)	68 (65-71)	66 (64-69)	29 (27-32)	56 (53-58)	43 (40-46)	42 (40-44)	62 (56-67)	53 (46-61)
Smoker, %	11 (10-13)	18 (17-19)	20 (18-23)	21 (18-25)	26 (23-29)	26 (24-29)	25 (22-27)	20 (18-23)	19 (18-21)	24 (22-26)	20 (15-25)	21 (18-24)
Non-smoker, %	80 (78-82)	72 (70-74)	66 (63-69)	74 (71-78)	63 (60-66)	59 (56-61)	54 (51-57)	64 (62-67)	66 (64-67)	60 (58-62)	66 (60-71)	66 (61-70)
Ex-smoker, %	9 (7-10)	10 (9-11)	14 (12-16)	5 (3-6) <sup>a</sup>	11 (9-13)	15 (13-17)	21 (18-23)	15 (13-18)	15 (13-16)	16 (15-18)	15 (10-19)	14 (12-16)

BMI, body mass index; WC, waist circumference. Values are expressed as mean (95% confidence interval).

<sup>a</sup> Ex-smoker for > 6 months.

the autonomous community where the study was conducted (correlation coefficient, 0.9,  $P < .001$ , and 0.82,  $P = .004$  for obesity and glucose level  $\geq 126$  mg/dL, respectively). In men, this correlation was significant for glucose level  $\geq 126$  mg/dL (correlation coefficient, 0.7,  $P = .025$ ), whereas obesity did not achieve statistical significance (correlation coefficient, 0.5).

## DISCUSSION

The distribution of most cardiovascular risk factors presents < 20% variability in the population aged 35-74 years in the Spanish autonomous communities. Our results put standardized prevalence of HBP at 43% and of dyslipidemia (total cholesterol  $\geq 250$  mg/dL) at 41%. Finally, > 25% of the population were smokers, 29% were obese, and 13% had diabetes. Over 75% of the population were far from the cutoff points of total cholesterol < 190 mg/dL or LDLc < 115 mg/dL proposed by the more demanding clinical practice guidelines.<sup>24</sup> These data improve our understanding of risk factor prevalence in the current century. They add information obtained with a more rigorous methodology than that used previously.<sup>8,9</sup> The low incidence of coronary disease and high life expectancy associated with being born into the Spanish population<sup>1</sup> suggest that aspects of the underlying mechanisms of coronary disease development should be studied in greater depth.

We found no great differences between the autonomous communities in prevalence of diabetes mellitus, HBP, dyslipidemia, obesity, and tobacco use, with coefficients of variation ranging from 7% to 26%. Geographical variability in prevalence of tobacco use, diabetes mellitus, and dyslipidemia with total cholesterol > 250 mg/dL was similar to that reported in the ERICE study, conducted with data from the 1990's.<sup>8</sup> Prevalence of total cholesterol > 200 mg/dL was significantly less variable in DARIOS than in ERICE (CV, 10% and 22%,  $P = .003$ ), whereas prevalence of HBP (CV, 18% and 8%,  $P < .001$ ) and obesity (CV, 19% and 13%,  $P = .021$ ) was significantly more variable in DARIOS. The autonomous communities of the Canary Islands, Andalusia, and Extremadura stand out for the greater prevalence of obesity, diabetes mellitus, HBP, or dyslipidemia in both men and women. Moreover, they also present greater mortality for ischemic heart disease than the other communities in the component studies.

Differences in age range, method of standardization, and the absence of laboratory cross-validation makes it difficult to compare our results with those of other, similar studies.<sup>8,9</sup> Despite this, our results indicate greater prevalence of obesity and diabetes mellitus in the first decade of the 21st century than that reported some decades ago.<sup>8,9</sup> Both cardiovascular risk factors correlate with mortality from ischemic heart disease in the population aged 35-74 years in the autonomous communities, especially among women. The ecological nature of this relationship prevents us from making definitive conclusions about the consequences of this finding. Should they be confirmed, these results would indicate we need a more intensive approach to the prevention of obesity and diabetes mellitus in Spain. Cohort studies with long-term follow-up are needed to provide greater insight into the role of both of these cardiovascular risk factors in the development of ischemic heart disease.

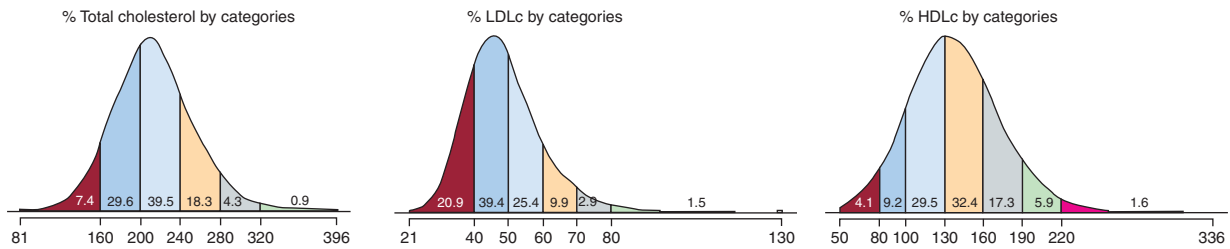
In DARIOS, prevalence of HBP and nondiagnosed diabetes mellitus was lower than that observed previously.<sup>3</sup> It has fallen from approximately 56% and 43% in the 1990's to 38% and 26% currently in hypertensive men and women, respectively; and from 28% and 21% to 19% and 10%, respectively, in men and women with diabetes. The screening for both illnesses, encouraged by the Spanish Society of Family and Community Medicine's Program of Preventative Activities and Health Promotion,<sup>26</sup> together with the

**Table 4**  
Lipid Profile and Prevalence of Dyslipidemia Standardized to the European Population by Component Study and General Study in Men and Women Aged 35-74 Years

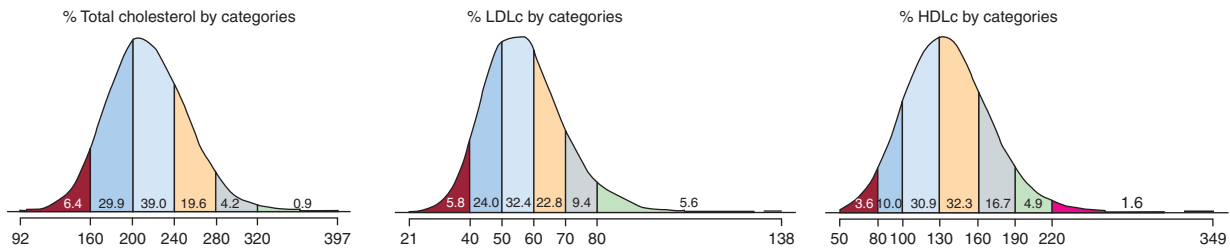
	ARTPER (45-74 years)	CDC	CORSAIB	DINO	DRECA-2	HERMEX	PREDIMERC	RECCyL	REGICOR	RIVANA	TALAVERA	General
<i>Men, n</i>	1493	2054	804	443	736	1046	966	1198	2685	1765	235	13 425
TC, mg/dL	212 (210-214)	211 (209-213)	217 (214-219)	215 (211-219)	214 (212-217)	226 (224-229)	222 (220-225)	207 (205-209)	210 (208-211)	217 (215-219)	227 (222-233)	216 (213-229)
HDLc, mg/dL	50 (49-51)	48 (47-48)	47 (47-48)	49 (48-50)	50 (49-50)	53 (52-53)	46 (45-47)	48 (48-49)	47 (47-48)	49 (49-50)	52 (51-53)	49 (48-50)
HDLc < 40 mg/dL, %	18 (16-20)	23 (21-25)	25 (22-28)	19 (16-23)	17 (15-20)	10 (9-12)	26 (23-29)	20 (17-22)	27 (25-29)	18 (16-20)	11 (7-16)	20 (16-23)
LDLc, mg/dL	136 (134-138)	134 (132-136)	139 (136-141)	142 (138-145)	134 (132-137)	149 (146-151)	150 (148-153)	130 (128-132)	138 (137-140)	143 (141-145)	151 (147-156)	140 (137-144)
Triglycerides, mg/dL	140 (135-145)	152 (147-157)	163 (155-170)	140 (130-151)	158 (151-166)	133 (127-138)	139 (133-144)	150 (144-155)	130 (126-133)	132 (128-136)	125 (115-136)	142 (135-149)
Diagnosed DL, %	59 (57-62)	35 (33-37)	25 (22-28)	33 (28-38)	34 (30-37)	31 (28-34)	36 (33-39)	27 (24-29)	34 (32-36)	36 (34-38)	39 (32-46)	35 (30-41)
Real DL, %												
TC < 190 mg/dL, %	85 (83-87)	75 (73-78)	75 (72-78)	81 (78-85)	81 (78-84)	88 (86-90)	87 (84-89)	73 (71-76)	75 (73-77)	81 (79-83)	88 (84-93)	81 (78-84)
TC < 240 mg/dL, %	64 (61-66)	44 (41-46)	40 (37-43)	46 (41-51)	48 (44-51)	53 (50-56)	50 (47-53)	35 (32-38)	42 (40-44)	46 (43-48)	53 (46-60)	47 (42-52)
TC < 250 mg/dL, %	62 (59-64)	41 (38-43)	34 (31-38)	41 (36-46)	43 (40-47)	46 (43-49)	46 (42-49)	33 (30-35)	40 (38-42)	42 (40-45)	49 (42-56)	43 (38-48)
LDLc < 115 mg/dL, %	84 (82-86)	73 (71-75)	73 (70-76)	81 (77-84)	78 (75-81)	87 (84-89)	86 (83-88)	69 (66-71)	73 (72-75)	79 (77-81)	88 (83-93)	79 (75-83)
LDLc < 160 mg/dL, %	65 (62-67)	44 (42-47)	40 (37-44)	50 (45-55)	48 (44-51)	55 (52-58)	54 (51-57)	36 (33-39)	45 (43-47)	49 (46-51)	56 (49-63)	49 (44-54)
<i>Women, n</i>	1739	2661	865	502	863	1158	1037	1238	3009	2097	293	15 462
TC, mg/dL	222 (221-224)	210 (209-212)	215 (213-218)	216 (213-219)	216 (214-219)	225 (223-227)	225 (222-227)	204 (202-206)	209 (208-211)	216 (215-218)	219 (215-224)	216 (212-220)
HDLc, mg/dL	60 (59-61)	54 (54-55)	56 (55-57)	59 (58-60)	59 (58-59)	60 (59-61)	54 (54-55)	56 (55-56)	57 (56-57)	59 (59-60)	60 (59-62)	58 (56-59)
HDLc < 50 mg/dL, %	25 (23-27)	41 (39-43)	31 (27-34)	24 (20-28)	24 (22-27)	21 (19-23)	39 (36-42)	31 (28-33)	32 (30-33)	21 (20-23)	19 (14-24)	28 (24-32)
LDLc, mg/dL	140 (138-141)	132 (131-134)	136 (134-139)	137 (134-140)	135 (133-137)	145 (143-147)	150 (147-152)	126 (124-128)	134 (132-135)	138 (137-140)	141 (137-145)	138 (134-141)
Triglycerides, mg/dL	118 (115-121)	123 (120-126)	117 (113-121)	101 (97-106)	117 (113-121)	102 (99-105)	108 (105-112)	113 (110-115)	98 (96-100)	97 (94-99)	94 (88-101)	108 (102-114)
Diagnosed DL, %	58 (55-60)	39 (37-41)	25 (22-27)	31 (27-36)	28 (25-31)	29 (26-31)	30 (28-33)	24 (21-26)	29 (27-31)	30 (28-32)	26 (21-31)	32 (26-38)
Real DL, %												
TC < 190 mg/dL, %	89 (87-90)	75 (74-77)	76 (73-79)	83 (79-86)	78 (76-81)	86 (84-88)	84 (82-86)	70 (68-73)	71 (69-72)	79 (77-80)	82 (77-87)	79 (75-83)
TC < 240 mg/dL, %	65 (62-67)	45 (43-47)	36 (33-39)	43 (38-47)	42 (39-45)	49 (46-52)	47 (44-50)	32 (29-34)	38 (36-40)	42 (40-44)	43 (38-49)	44 (38-49)
TC < 250 mg/dL, %	62 (60-64)	43 (41-45)	32 (29-35)	39 (34-43)	38 (35-42)	43 (41-46)	42 (39-45)	28 (25-30)	35 (34-37)	37 (35-39)	37 (32-43)	40 (34-45)
LDLc < 115 mg/dL, %	85 (83-87)	72 (70-74)	71 (68-74)	78 (75-82)	73 (70-76)	84 (82-86)	82 (80-84)	66 (63-68)	67 (65-69)	76 (74-77)	79 (74-84)	76 (71-80)
LDLc < 160 mg/dL, %	64 (62-66)	45 (43-47)	35 (32-38)	43 (39-48)	42 (38-45)	49 (46-51)	49 (46-52)	31 (29-34)	39 (37-41)	42 (40-44)	41 (35-47)	44 (38-49)

DL, dyslipidemia; HDLc, high density lipoprotein cholesterol; LDLc, low density lipoprotein cholesterol; Real DL, diagnosed DL + TC or LDLc above the limit indicated or HDLc below the value indicated; TC, total cholesterol. Values are expressed as mean (95% confidence interval).

Panel A. Men



Panel B. Women



**Figure 2.** Population-wide distribution of total cholesterol, high density lipoprotein cholesterol and low density lipoprotein cholesterol in the population aged 35–74 years in the DARIOS study. HDLc, high density lipoprotein cholesterol; LDLc, low density lipoprotein cholesterol.

**Table 5.** Comparison of Prevalence Stratified by Age Between DARIOS and the National Health Survey 2006 (NHS 2006)

	Smoker		High blood pressure		Dyslipidemia		Obesity		Type II diabetes mellitus	
	DARIOS	NHS 2006	DARIOS	NHS 2006	DARIOS*	NHS 2006	DARIOS	NHS 2006	DARIOS	NHS 2006
<b>Men</b>										
35–44 years	40%	41%	24%	10%	32%	14%	22%	15%	5%	1%
45–54 years	38%	41%	42%	20%	46%	21%	30%	21%	14%	1%
55–64 years	29%	31%	61%	38%	49%	29%	33%	21%	23%	6%
65–74 years	22%	21%	72%	44%	47%	31%	30%	26%	29%	14%
<b>Women</b>										
35–44 years	36%	34%	12%	8%	19%	7%	15%	12%	3%	2%
45–54 years	26%	31%	31%	18%	37%	17%	26%	16%	8%	4%
55–64 years	9%	13%	55%	35%	55%	31%	38%	24%	16%	9%
65–74 years	3%	5%	72%	56%	59%	37%	44%	29%	24%	16%

\* Total cholesterol  $\geq 250$  mg/dL.

contract programs of several autonomous communities, may have played a key role in this.

In DARIOS, prevalence of diabetes mellitus, HBP, and dyslipidemia differed substantially from that obtained by the 2006 NHS<sup>6</sup> (Table 5). This difference may be due to the fact that DARIOS obtained information via questionnaires, which was complemented by blood tests (lipids and glucose level) and measurements of blood pressure, weight, height, and waist circumference. Nonetheless, prevalence estimated exclusively from self-reported information (eg, tobacco use) was similar in both DARIOS and the NHS.<sup>7</sup>

**Characteristics and Limitations of the Study**

The DARIOS study includes 11 studies with population-based random samples conducted in the first decade of the 21st century. Despite the fact that not all of Spain is covered in the study, the

sample appears to be representative of approximately 70% of the Spanish population aged 35–74 years. Furthermore, the response rate was generally good (73%); in only 3 studies (representing 21% of participants) was it  $< 70\%$ . We do not believe the use of healthcare ID cards in 6 of the 11 studies constitutes a selection bias, as  $> 98\%$  of the population uses public health services, according to the NHS.<sup>7</sup>

All the component studies followed a standard WHO method<sup>20</sup> and took measurements with calibrated apparatus. Moreover, we performed an analysis of concordance of lipid profile results using a reference laboratory to correct the few deviations observed. Lipid values prior to standardization and adaptation can be consulted in individual study reports.<sup>3,10–19</sup> Prevalence of HBP based on 2 blood pressure measurements presented differences if it was calculated from the mean of both or if only the lower of the two measurements was used. In order to minimize the “white-coat” effect,<sup>31</sup> we chose the lower of the 2 blood pressure measurements.



## CONCLUSIONS

In the Spanish population aged 35-74 years, standardized prevalence of HBP and dyslipidemia was > 40%; for obesity and tobacco use, 27%; and for diabetes, 13% in the first decade of the 21st century. Variability between autonomous communities in prevalence of cardiovascular risk factors was relatively low, although differences between those areas with the most extreme levels of prevalence were considerable. The Canary Islands, Extremadura, and Andalusia had a greater accumulation of significantly more prevalent factors than the mean for the 11 component studies.

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## CONFLICTS OF INTEREST

None declared.

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