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Original article

Metabolic Syndrome in Spain: Prevalence and Coronary Risk Associated With Harmonized Definition and WHO Proposal. DARIOS Study

Daniel Fernández-Bergés,[a,*] Antonio Cabrera de León,[b,c] Héctor Sanz,[d] Roberto Elosua,[d,e] María J. Guembe,[f,g] Maite Alzamora,[h,i] Tomás Vega-Alonso,[j] Francisco J. Félix-Redondo,[a,k] Honorato Ortiz-Marrón,[l] Fernando Rigo,[m] Carmen Lama,[n,o] Diana Gavrila,[e,p] Antonio Segura-Fragoso,[q] Luis Lozano,[a] and Jaume Marrugat[d]

[a] *Unidad de Investigación Don Benito Villanueva, Programa de Investigación en Enfermedades Cardiovasculares (PERICLES), Fundesalud, Gerencia Área Sanitaria Don Benito-Villanueva, Badajoz, Spain*
[b] *Unidad de Investigación de Atención Primaria, Hospital Universitario Nuestra Señora de Candelaria, Santa Cruz de Tenerife, Spain*
[c] *Área de Medicina Preventiva y Salud Pública, Universidad de La Laguna, La Laguna, Santa Cruz de Tenerife, Spain*
[d] *Grupo de Epidemiología y Genética Cardiovascular, Programa de Investigación en Procesos Inflamatorios y Cardiovasculares, Instituto Municipal de Investigación Médica, Barcelona, Spain*
[e] *CIBER Epidemiología y Salud Pública (CIBERESP), Spain*
[f] *Servicio de Docencia y Desarrollo Sanitarios, Departamento de Salud, Gobierno de Navarra, Pamplona, Navarra, Spain*
[g] *Grupo de Investigación Riesgo Vascular en Navarra (RIVANA), Departamento de Salud, Gobierno de Navarra, Pamplona, Navarra, Spain*
[h] *Centre de Salud Riu Nord-Riu Sud, Institut Català de la Salut, Santa Coloma de Gramenet, Barcelona, Spain*
[i] *USR Metropolitana Nord, ICS-IDIAP Jordi Gol, Mataró, Barcelona, Spain*
[j] *Dirección General de Salud Pública e Investigación, Desarrollo e Innovación, Consejería de Sanidad de la Junta de Castilla y León, Valladolid, Spain*
[k] *Centro de Salud Villanueva Norte, Servicio Extremeño de Salud, Villanueva de la Serena, Badajoz, Spain*
[l] *Servicio de Epidemiología, Subdirección General de Promoción de la Salud y Prevención, Servicio Madrileño de Salud, Madrid, Spain*
[m] *Grupo Cardiovascular de Baleares de redIAPP, UB Genova, IB-Salut, Palma de Mallorca, Baleares, Spain*
[n] *Gestión y Evaluación, Dirección General de Asistencia Sanitaria, Servicio Andaluz de Salud, Spain*
[o] *CIBER de Fisiopatología de la Obesidad y la Nutrición, Instituto de Salud Carlos III, Madrid, Spain*
[p] *Servicio de Epidemiología, Consejería de Sanidad y Consumo de la Región de Murcia, Murcia, Spain*
[q] *Servicio de Investigación, Instituto de Ciencias de la Salud de Castilla-La Mancha, Talavera de la Reina, Toledo, Spain*

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ABSTRACT

Introduction and objectives: To update the prevalence of metabolic syndrome and associated coronary risk in Spain, using the harmonized definition and the new World Health Organization proposal (metabolic premorbid syndrome), which excludes diabetes mellitus and cardiovascular disease.
Methods: Individual data pooled analysis study of 24 670 individuals from 10 autonomous communities aged 35 to 74 years. Coronary risk was estimated using the REGICOR function.
Results: Prevalence of metabolic syndrome was 31% (women 29% [95% confidence interval, 25%-33%], men 32% [95% confidence interval, 29%-35%]). High blood glucose (P=.019) and triglycerides (P<.001) were more frequent in men with metabolic syndrome, but abdominal obesity (P<.001) and low high-density lipoprotein cholesterol (P=.001) predominated in women. Individuals with metabolic syndrome showed moderate coronary risk (8% men, 5% women), although values were higher (P<.001) than in the population without the syndrome (4% men, 2% women). Women and men with metabolic syndrome had 2.5 and 2 times higher levels of coronary risk, respectively (P<.001). Prevalence of metabolic premorbid syndrome was 24% and the increase in coronary risk was also proportionately larger in women than in men (2 vs 1.5, respectively; P<.001).
Conclusions: Prevalence of metabolic syndrome is 31%; metabolic premorbid syndrome lowers this prevalence to 24% and delimits the population for primary prevention. The increase in coronary risk is proportionally larger in women, in both metabolic syndrome and metabolic premorbid syndrome.
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* Corresponding author: Unidad de Investigación Don Benito Villanueva, Programa de Investigación en Enfermedades Cardiovasculares (PERICLES), Fundesalud, Gerencia Área Sanitaria Don Benito-Villanueva, Plaza de Conquistadores 49-50, 06700 Villanueva de la Serena, Badajoz, Spain.
E-mail address: polonibo@gmail.com (D. Fernández-Bergés).

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Síndrome metabólico en España: prevalencia y riesgo coronario asociado a la definición armonizada y a la propuesta por la OMS. Estudio DARIOS

Palabras clave:
Síndrome metabólico
Diabetes mellitus
Enfermedad cardiovascular
Funciones de riesgo

RESUMEN

Introducción y objetivos: Actualizar la prevalencia del síndrome metabólico en España y su riesgo coronario asociado, empleando la definición armonizada y la nueva propuesta de la Organización Mundial de la Salud (síndrome metabólico premórbido), que excluye diabetes mellitus y enfermedad cardiovascular.

Métodos: Análisis agrupado con datos individuales de 11 estudios, incluyendo a 24.670 individuos de 10 comunidades autónomas con edad 35-74 años. El riesgo coronario se estimó con la función REGICOR.

Resultados: La prevalencia de síndrome metabólico fue del 31% (mujeres, 29%; intervalo de confianza del 95%, 25-33%; varones, 32%; intervalo de confianza del 95%, 29-35%). Entre los varones con síndrome metabólico, fueron más frecuentes la elevación de glucemia ($p = 0{,}019$) y triglicéridos ($p < 0{,}001$); por contra, entre las mujeres predominaron obesidad abdominal ($p < 0{,}001$) y colesterol unido a las lipoproteínas de alta densidad bajo ($p = 0{,}001$). Las personas con síndrome metabólico mostraron riesgo coronario moderado (varones, 8%; mujeres, 5%), pero mayor ($p < 0{,}001$) que la población sin síndrome metabólico (varones, 4%; mujeres, 2%). El incremento de riesgo coronario asociado al síndrome metabólico fue mayor en mujeres que en varones (2,5 frente a 2 veces, respectivamente; $p < 0{,}001$). La prevalencia de síndrome metabólico premórbido fue del 24% y su riesgo coronario asociado también aumentó más en las mujeres que en los varones (2 frente a 1,5; $p < 0{,}001$).

Conclusiones: La prevalencia de síndrome metabólico es del 31%; el síndrome metabólico premórbido la rebaja al 24% y delimita la población para prevención primaria. El incremento de riesgo coronario es proporcionalmente mayor en las mujeres, tanto en síndrome metabólico como en síndrome metabólico premórbido.

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Abbreviations

CR: coronary risk
CVD: cardiovascular disease
DM: diabetes mellitus
HDL-C: high-density lipoprotein cholesterol
MS: metabolic syndrome
MPMS: metabolic premorbid syndrome

INTRODUCTION

The term "metabolic syndrome" (MS) emerged 30 years ago to define a nonrandom grouping of factors of metabolic origin which were frequently observed in clinical practice.[1] Those factors were abdominal obesity, dyslipidemia, high blood sugar, and high blood pressure. Few clinical concepts over the last 20 years have been so controversial,[2,3] although the controversy did lead to the publication of an international consensus[4] that has enjoyed great success. Using the harmonized definition, the prevalence of MS is about 30% of the adult population in developed countries.[5]

However, in a subsequent paper sponsored by the World Health Organization (WHO), a proposal was made to exclude individuals who already have diabetes mellitus (DM) and cardiovascular disease (CVD) because MS cannot be used for primary prevention in those individuals.[6] The resulting condition could be termed metabolic premorbid syndrome (MPMS), and its prevalence and impact have not been investigated in the Spanish general population to date.

The DARIOS study documented the spread of obesity and DM in Spain during the first decade of this century, and compared the results to previous decades.[7] The spread of these two conditions is a global trend from which no society appears to be immune, with an increase in obesity being seen in all regions of the world over the last 30 years.[8] The rise in obesity is in turn inseparable from the increase in DM,[9] and a further consequence of the epidemic is an increased prevalence of MS. However, not all individuals with MS have the same combination of diagnostic criteria and it has been shown that different combinations of criteria are associated with different levels of CVD risk.[10]

The objectives of this study were to update the prevalence of MS in Spain using the harmonized definition and the definition of MPMS, and to analyze the associated coronary risk (CR).

METHODS

Study Population

We performed a pooled analysis of individual data from 11 population studies carried out in 10 autonomous communities (DARIOS study). The studies were ARTPER (Catalonia-Barcelona), CDC de Canarias (Canary Islands), CORSAIB (Balearic Islands), DINO (Region of Murcia), RBEC-2 (Andalusia), HERMEX (Extremadura), PREDIMERC (Community of Madrid), RECCyL (Castile and León), REGICOR (Catalonia, Girona), RIVANA (Chartered Community of Navarre), and TALAVERA (Castile-La-Mancha). They all included individuals aged between 35 and 74 years, except for the ARTPER study, which included participants from 49 to 74 years. In each study, all subjects were informed of the objectives and provided signed consent to participate. The methodology has been described previously.[7] DARIOS was approved by the Clinical Research Ethics Committee of the Municipal Institute of Health Care (Barcelona).

Variables Studied

In addition to age and sex, we collected data on level of education, self-reported tobacco use, and history of DM and CVD. We measured waist circumference, weight, and height, and estimated the body mass index by dividing weight in kilos by height squared in meters. All blood samples were obtained after

Table 1
Population Characteristics of Each Component Study for the Population Aged 35-74 Years, by Metabolic Status. Coronary Risk and Standardized Prevalence of Metabolic Syndrome and Metabolic Premorbid Syndrome

	ARTPER[a] Catalonia		CDC Canary Islands		CORSAIB Balearic Islands		DINO Region of Murcia		DRECA-2 Andalusia		HERMEX Extremadura		PREDIMERC Community of Madrid		RECCyL Castile and León		REGICOR Catalonia		RIVANA Chartered Community of Navarre		TALAVERA Castile-La-Mancha		Total DARIOS[b]		
Men	No MS (n=849)	MS (n=644)	No MS (n=1387)	MS (n=667)	No MS (n=507)	MS (n=297)	No MS (n=310)	MS (n=133)	No MS (n=507)	MS (n=229)	No MS (n=688)	MS (n=358)	No MS (n=685)	MS (n=281)	No MS (n=828)	MS (n=370)	No MS (n=559)	MS (n=160)	No MS (n=1202)	MS (n=563)	No MS (n=163)	MS (n=72)	Sin SM (n=7685)	SM (n=3774)	P^c
Primary education	539 (66%)	417 (68%)	851 (62%)	483 (73%)	352 (69%)	226 (77%)	192 (62%)	99 (74%)	—	—	413 (61%)	215 (61%)	131 (19%)	86 (31%)	—	—	267 (48%)	89 (56%)	915 (76%)	457 (81%)	115 (71%)	56 (78%)	56 (49-65)	65 (59-73)	.103
University	50 (6%)	30 (5%)	199 (14%)	44 (7%)	61 (12%)	20 (7%)	59 (19%)	20 (15%)	—	—	75 (11%)	29 (8%)	194 (28%)	56 (20%)	—	—	127 (23%)	26 (16%)	176 (15%)	60 (11%)	9 (6%)	1 (1%)	14 (10-18)	9 (7-14)	.116
Smoker	261 (31%)	204 (32%)	469 (34%)	198 (30%)	194 (38%)	100 (34%)	101 (33%)	39 (30%)	168 (33%)	63 (28%)	275 (40%)	122 (34%)	185 (27%)	86 (31%)	262 (32%)	118 (32%)	183 (33%)	49 (31%)	380 (32%)	224 (40%)	43 (26%)	19 (26%)	33 (31-35)	32 (30-35)	.688
Diabetes	122 (14%)	258 (40%)	105 (8%)	138 (21%)	36 (7%)	71 (24%)	22 (10%)	29 (28%)	26 (5%)	82 (36%)	52 (8%)	71 (20%)	47 (7%)	54 (19%)	28 (3%)	68 (18%)	44 (8%)	49 (31%)	83 (7%)	98 (17%)	12 (7%)	24 (33%)	7 (6-9)	25 (20-31)	<.001
CVD	97 (11%)	118 (18%)	70 (5%)	55 (8%)	40 (8%)	44 (15%)	—	—	26 (5%)	36 (16%)	24 (3%)	41 (12%)	76 (11%)	35 (13%)	36 (4%)	40 (11%)	18 (3%)	11 (7%)	63 (5%)	56 (10%)	9 (6%)	7 (10%)	6 (4-8)	12 (10-14)	<.001
10-year CR	5 [4-8]	8 [6-12]	2 [2-4]	5 [4-8]	4 [2-7]	7 [4-11]	—	—	1 [1-2]	4 [3-6]	3 [2-5]	6 [4-10]	3 [2-6]	7 [4-11]	2 [1-3]	4 [3-6]	3 [2-5]	7 [4-9]	3 [2-5]	6 [4-10]	4 [2-7]	7 [4-10]	4 [4-5]	8 [7-8]	<.001
10-year CR (n analyzed)	765	560	1.381	663	504	295	0	0	466	193	670	325	617	253	771	338	543	151	1.160	519	150	66	7.027	3.363	
Standardized prevalence of MS[d]	42 (39-45)		34 (31-36)		36 (33-39)		29 (25-34)		30 (27-33)		33 (31-36)		29 (26-31)		30 (27-33)		23 (20-25)		32 (30-34)		28 (22-34)		32 (29-35)		
Standardized prevalence of MPMS[d]	32 (28-35)		28 (25-30)		29 (25-33)		—		21 (18-25)		29 (26-32)		25 (22-28)		25 (22-28)		18 (15-21)		27 (25-30)		21 (15-27)		26 (23-28)		
Women	No MS (n=999)	MS (n=740)	No MS (n=1765)	MS (n=896)	No MS (n=577)	MS (n=288)	No MS (n=362)	MS (n=140)	No MS (n=615)	MS (n=248)	No MS (n=805)	MS (n=353)	No MS (n=783)	MS (n=254)	No MS (n=825)	MS (n=413)	No MS (n=583)	MS (n=175)	No MS (n=1634)	MS (n=463)	No MS (n=205)	MS (n=88)	No MS (n=9153)	SM (n=4058)	P^c
Primary education	697 (73%)	540 (77%)	1075 (61%)	719 (81%)	429 (74%)	240 (84%)	244 (68%)	113 (81%)	–	–	460 (58%)	207 (59%)	195 (25%)	140 (55%)	—	—	259 (45%)	123 (70%)	1177 (72%)	418 (90%)	145 (71%)	62 (71%)	58 (51-66)	74 (68-80)	.002
University	30 (3%)	9 (1%)	235 (13%)	41 (5%)	52 (9%)	5 (2%)	44 (12%)	2 (1%)	–	–	105 (13%)	12 (3%)	156 (20%)	17 (7%)	—	—	132 (23%)	15 (9%)	218 (13%)	16 (3%)	9 (4%)	3 (3%)	11 (9-15)	4 (2-5)	<.001
Smoker	114 (11%)	55 (7%)	423 (24%)	106 (12%)	129 (22%)	30 (10%)	89 (25%)	16 (12%)	167 (27%)	50 (20%)	253 (31%)	45 (13%)	202 (26%)	41 (16%)	177 (22%)	42 (10%)	127 (22%)	18 (10%)	423 (26%)	74 (16%)	37 (18%)	8 (9%)	23 (20-26)	12 (10-15)	<.001
Diabetes	47 (5%)	251 (34%)	74 (4%)	220 (25%)	19 (3%)	74 (26%)	10 (4%)	36 (29%)	22 (4%)	85 (35%)	19 (2%)	109 (31%)	16 (2%)	52 (20%)	7 (1%)	68 (16%)	18 (3%)	41 (23%)	60 (4%)	97 (21%)	6 (3%)	30 (34%)	3 (3-4)	26 (23-30)	<.001
CVD	43 (4%)	81 (11%)	36 (2%)	64 (7%)	13 (2%)	19 (7%)	—	—	6 (1%)	26 (10%)	4 (0%)	24 (7%)	92 (12%)	36 (14%)	18 (2%)	13 (3%)	9 (2%)	5 (3%)	31 (2%)	35 (8%)	0 (0%)	6 (7%)	2 (1-4)	7 (6-10)	<.001
10-year CR	3 [2-3]	5 [4-7]	1 [1-2]	4 [3-6]	2 [1-3]	5 [3-7]	—	—	1 [1-2]	4 [3-6]	1 [1-2]	4 [3-6]	1 [1-3]	5 [3-7]	2 [1-3]	4 [3-6]	1 [1-2]	4 [3-6]	1 [1-3]	4 [3-6]	2 [1-3]	5 [3-7]	2 [2-2]	5 [5-5]	<.001
10-year CR (no. analyzed)	963	682	1754	891	566	286	0	0	594	223	793	332	700	224	762	392	576	172	1621	440	195	82	8524	3724	

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Table 1 *(Continued)*
Population Characteristics of Each Component Study for the Population Aged 35-74 Years, by Metabolic Status. Coronary Risk and Standardized Prevalence of Metabolic Syndrome and Metabolic Premorbid Syndrome

Women	No MS (n= 999)	MS (n= 740)	No MS (n= 1765)	MS (n= 896)	No MS (n=577)	MS (n= 288)	No MS (n= 362)	MS (n= 140)	No MS (n= 615)	MS (n= 248)	No MS (n= 805)	MS (n= 353)	No MS (n= 783)	MS (n= 254)	No MS (n= 825)	MS (n= 413)	No MS (n= 583)	MS (n= 175)	No MS (n= 1634)	MS (n= 463)	No MS (n= 205)	MS (n= 88)	No MS (n= 9153)	SM (n= 4058)	P^c
Standardized prevalence of MS[d]	41 (39-43)		37 (35-39)		31 (28-34)		27 (23-30)		27 (25-30)		29 (27-32)		23 (21-26)		31 (28-33)		25 (22-27)		22 (20-24)		25 (20-30)		29 (25-33)		
Standardized prevalence of MPMS[d]	31 (28-34)		30 (28-33)		26 (23-29)		–		21 (18-24)		23 (20-25)		20 (17-23)		27 (25-30)		21 (18-25)		18 (16-20)		19 (14-24)		24 (21-27)		

CVD, cardiovascular disease; CR, coronary risk; MS: metabolic syndrome; MPMS, metabolic premorbid syndrome.
Unless otherwise indicated, data are n (%), median [interquartile range].
[a] 49-74 years.
[b] Calculated by combining individual results using the DerSimonian-Laird method for random effects models. Figures are percentages with corresponding 95% confidence intervals.
[c] Comparison between patients with and without MS in the overall DARIOS sample.
[d] Standardized by age group using the European population as the reference population.

fasting >8 h, and triglycerides, glucose, and high-density lipoprotein cholesterol (HDL-C) were determined. Lipid values were corrected based on an analysis of concordance between the different studies in the pooled analysis and the DARIOS[7] reference laboratory. We used the lowest of two resting measurements of systolic and diastolic blood pressure.

The international consensus definition of MS[4] requires the presence of 3 of the following 5 criteria: *a)* high fasting glucose (≥100 mg/dL) or receiving treatment for diabetes with insulin or oral hypoglycemic agents; *b)* high systolic (≥130 mmHg) or diastolic (≥85 mmHg) blood pressure, or use of antihypertensive treatment; *c)* HDL-C <40 mg/dL (men) or <50 mg/dL (women); *d)* triglycerides ≥150 mg/dL, and *e)* waist circumference ≥102 cm (men) or ≥88 cm (women). MPMS[6] was defined by excluding participants with MS who had DM (previously diagnosed, or with fasting blood glucose ≥126 mg/dL) or with a history of CVD (based on individuals reporting prior acute myocardial infarction, angina, or stroke).

Ten-year CR was calculated using the REGICOR calibrated function[11] after excluding participants undergoing secondary prevention of CVD.

Statistical Analysis

Categorical variables were summarized as absolute frequencies and percentages, or proportions and 95% confidence intervals (95%CI). Comparisons were made using the χ^2 test. Prevalence of MS and MPMS were age-standardized using the direct method and taking the European population as the reference population.[12] After combining the estimated scores obtained in each of the component studies and compensating for the differences in sample size, we used the DerSimonian-Laird[13] method for random effects models to calculate the overall prevalence of each risk factor and the corresponding confidence intervals. Comparisons between groups of risk factors were performed using the Z test. The Mann-Whitney U test was used for comparisons between CR groups and CR was described using the median [interquartile range]. The relationship between sex and MS was analyzed, independently adjusting a linear regression model for each component study using the logarithm of CR as the response variable and further adjusting for age, sex, MS, and the interaction between sex and MS. Analyses were performed using version 2.11.1 of the R statistical program (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

The study included 24 670 participants from 10 autonomous communities representing approximately 70% of Spain's population aged 35 years to 74 years. Overall, 7832 of the participants had MS, with a prevalence of 32% (95%CI, 29-35) in males and 29% (95%CI, 25-33) in women. When the definition of MPMS was applied, the prevalence dropped by 20%, to 26% (95%CI, 23-28) in males and 24% (95%CI, 21-27) in females. On average, men with MS were 4 (1.5) years older than those without (57 vs 53 years, respectively, P=.046); in women the difference was 9 (1.5) years (60 vs 51 years, P<.001).

Table 1 describes the sample characteristics for each component study in terms of level of education, prevalence of smoking, DM, and CVD, according to whether MS was present or not. It also provides data on CR and the standardized prevalence of MS and MPMS for each autonomous community. After exclusion of the ARTPER study (due to the age of study participants), the highest prevalence of MS in men was observed in the Balearic Islands, the Canary Islands, and Extremadura; in women, the highest

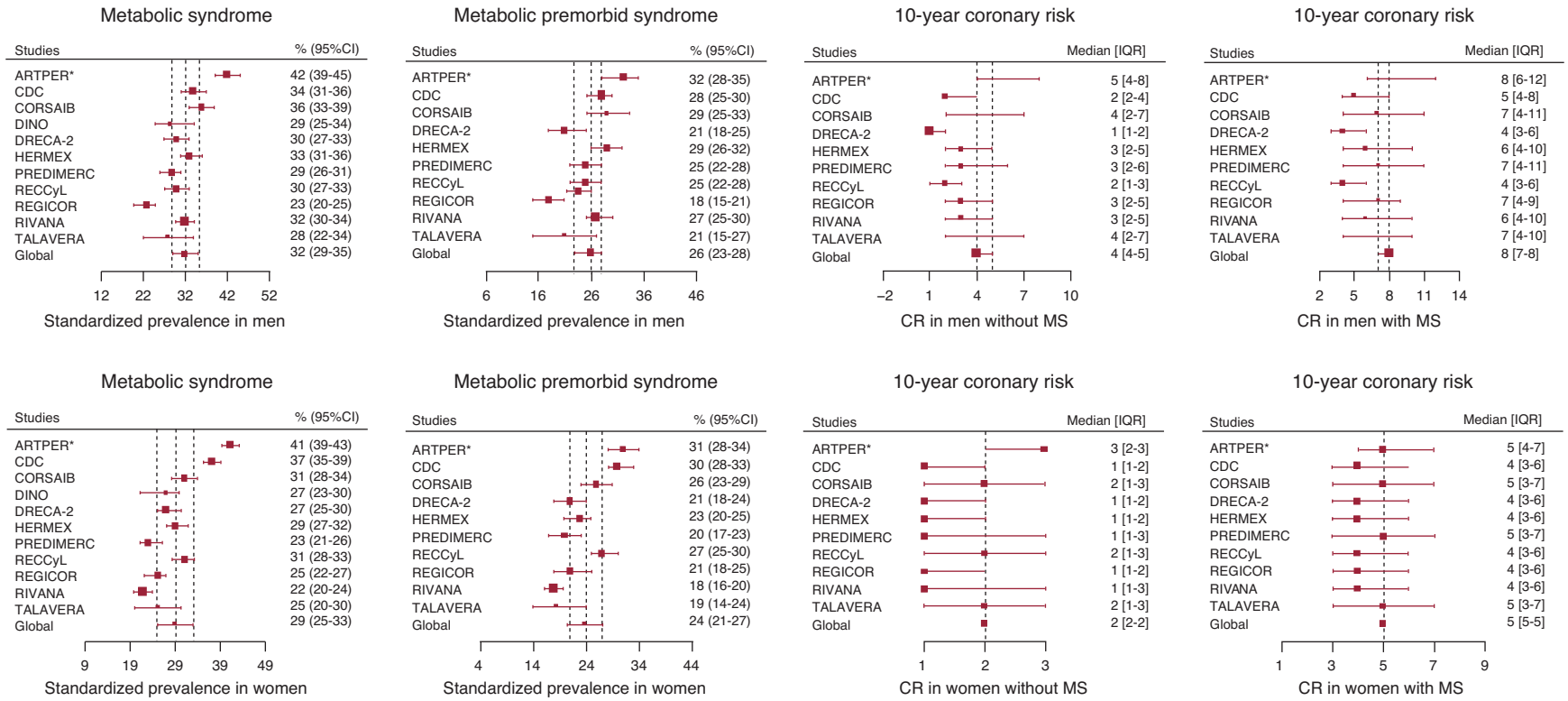

Figure. Prevalence of metabolic syndrome, metabolic premorbid syndrome, and coronary risk in population aged 35 to 74 years, stratified by sex, for each cohort. 95%CI, 95% confidence interval; CR, coronary risk; IQR, interquartile range; MS, metabolic syndrome. *Age 49-74 years.

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prevalence was observed in the Canary Islands, the Balearic Islands, and Castile and León. Prevalence of MPMS followed the same pattern. For Spain as a whole, when comparing all participants in the DARIOS study, we found that individuals with MS had a higher frequency of CVD and DM in both men and women ($P<.001$). Women with MS also had a lower prevalence of smoking ($P<.001$) and a lower educational level than those without MS, differences which were not observed in men.

Ten-year CR was significantly higher in men, both in individuals with MS (8% of men vs 5% of women, $P<.001$), those with MPMS (6% of men vs 4% of women, $P<.001$), and those without MS (4% of men vs 2% of women, $P<.001$). However, the increase in CR associated with presence of the syndrome was higher in women, both in MS (2.5-fold increase in women compared to a 2-fold increase in men, $P<.001$) and in MPMS (2-fold increase in women and 1.5-fold increase in men, $P<.001$). Men in Catalonia had the highest CR values among individuals with MS. The Figure shows the prevalence of the syndrome and associated CR for each cohort, stratified by sex.

Table 2 shows the distribution of MS criteria by sex in those with the syndrome. In women, the criteria of abdominal obesity ($P<.001$) and low HDL-C ($P=.001$), predominated, while in men these were high fasting glucose ($P=.019$) and high triglycerides ($P<.001$). High blood pressure was the only criterion which did not show significant differences by sex. The same distributional pattern by sex was repeated in all of the autonomous communities studied (supplementary material, Tables A and B).

Finally, Table 3 presents the prevalence of MS and MPMS by age group, with the associated CR in each stratum. Prevalence of both MS and MPMS increased with age, as did CR (trend, $P<.001$). However, while MS and MPMS were more prevalent in males up to the age of 54 years, prevalence rates balanced out between the sexes in the 55 to 64 age group, and were higher in women from the age of 65 years onwards. Using the definition of MPMS led to a 20% reduction in prevalence, with the reduction being statistically significant from 45 years of age onwards ($P<.001$). Median CR values were high (>10%) only in men with MS aged >64 years.

DISCUSSION

The nearly 8000 people with MS studied here represent the largest sample with the syndrome analyzed to date in Spain. Furthermore, this study analyzes CR associated with the syndrome across most of the country, and is the first to introduce the concept of MPMS. Using the harmonized definition, MS affected a third of the adult population in the first decade of the century, and CR ranged from a low level in those without the syndrome to moderate levels. Using the concept of MPMS, whereby individuals with DM or CVD are excluded from the definition of the syndrome, focuses clinical use of the syndrome on primary prevention of both diseases and significantly reduces the target population; it also defines a younger population, as those excluded are generally in older age groups.

As in other countries,[14] MS was slightly more prevalent in men. Interestingly though, while MS was significantly more prevalent in men up to the age of 54 years, we found that prevalence rates balanced out by sex in 55- to 64-year-olds because prevalence in women increased at twice the rate in men in that age group. Beyond the age of 65 years, prevalence did not increase in men but continued to increase in women, becoming significantly higher than in men during the last decades of life. This effect may well be linked to the disappearance of estrogen protection after menopause which, together with the lipid changes that occur at that time of life, leads to increased CVD in women.[15] Such differences may partly explain the uneven increase in CR; although always proportionally higher in women, the risk does not reach the same levels as men. Qiao et al.[16] applied the pre-international consensus

Table 2
Distribution by Sex of Metabolic Syndrome Criteria According to Presence of the Syndrome (n=7832)

	MS			MPMS		
	Men, % (95%CI)	Women, % (95%CI)	*P*	Men, % (95%CI)	Women, % (95%CI)	*P*
Abdominal circumference ≥102 cm (men) or ≥88 cm (women)	77 (73-81)	95 (93-97)	<.001	76 (71-82)	94 (92-96)	<.001
HDL-C <40 mg/dL (1.0 mmol/l) (men) or <50 mg/dl (1.3 mmol/l) (women)	41 (36-47)	58 (52-65)	<.001	43 (37-50)	60 (53-68)	.001
Fasting glucose ≥100 mg/dL or drug treatment	80 (76-84)	71 (65-77)	.019	69 (64-76)	58 (51-67)	.036
Triglycerides ≥150 mg/dL	62 (57-67)	44 (39-49)	<.001	67 (61-72)	45 (39-51)	<.001
SBP ≥130 or DBP ≥85 mmHg or drug treatment	89 (87-92)	87 (83-90)	.162	88 (85-90)	85 (81-89)	.269

95%CI, 95% confidence interval; DBP, diastolic blood pressure; HDL-C, high-density lipoprotein cholesterol; MPMS, metabolic premorbid syndrome; MS, metabolic syndrome; SBP, systolic blood pressure.

Table 3
Prevalence of Metabolic Syndrome and Metabolic Premorbid Syndrome by Age Group, With Coronary Risk for Each Stratum

Age group	MS[a]				MPMS[a]				*P*[b]	
	Men		Women		Men		Women		Men	Women
	Prevalence	CR[c]	Prevalence	CR[c]	Prevalence	CR[c]	Prevalence	CR[c]		
35-44	19.7 (18.4-21.2)	3 [2-4]	10.9 (9.9-11.9)	1 [1-2]	18 (16.6-19.5)	3 [2-4]	10 (9-11)	1 [1-2]	.094	.219
45-54	31.7 (30-33.4)	5 [4-7]	24.9 (23.5-26.3)	4 [3-5]	26.6 (24.9-28.5)	5 [3-6]	21.1 (19.7-22.6)	3 [2-4]	<.001	<.001
55-64	40.6 (38.9-42.4)	8 [5-10]	42.1 (40.6-43.8)	5 [4-7]	32.3 (30.4-34.4)	7 [5-9]	33.8 (32.1-35.6)	5 [3-6]	<.001	<.001
65-74	42.2 (40.2-44.3)	11 [8-14]	52.5 (50.6-54.6)	5 [4-7]	31.5 (29.1-34.1)	9 [7-12]	40.4 (38-42.8)	4 [3-5]	<.001	<.001

CR, 10-year coronary risk; MS, metabolic syndrome; MPMS, metabolic premorbid syndrome.
Prevalences are shown as percentages (95% confidence intervals).
[a] The trend towards an increase with age was significant in men and women, both for prevalence and CR ($P<.001$).
[b] Comparison of prevalence of MS and MPMS in men and women.
[c] Median [interquartile range].

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definitions and found that MS predicted CVD mortality better in men than in women in the European population. Although we did not measure mortality, we did find that CR was higher in males.

We used a 10-year horizon when calculating CR, although MS may require longer than that to induce CVD; if that were the case, it might help explain why our CR values were not very high. The Spanish population also has some of the lowest CVD mortality in Europe,[17] a fact which seems to be reflected in our study, as participants without MS had a low CR (<5 in both sexes). On the other hand, the increased risk of CVD with MS has been demonstrated in the United States in the Framingham follow-up cohort.[18] While the cross-sectional nature of our study means that we cannot confirm those results, participants with MS in the DARIOS study did show a moderate rather than a low level of risk (≥5%). Using MPMS, the risk level increased to moderate in men, and the fact that the CR doubled in women with MPMS is noteworthy, even though the values remained low.

The distribution by sex of MS diagnostic criteria was similar across the different regions of Spain, with abdominal obesity being frequent in women and impaired fasting glucose in men. High blood pressure was prevalent in both sexes. These data coincide with reports from other Spanish studies.[19–22] We also found low levels of HDL-C in women and raised triglycerides in men, as previously observed in the Canary Islands.[23] This sex-based epidemiological pattern was not reversed in any of the autonomous communities studied, indicating a certain homogeneity within MS. These differences may be linked to the lifestyles of men and women, as there is some evidence from studies in children that dietary patterns and amount of physical activity impact differently on different MS criteria.[24] These differences may also contribute to the unequal increase in CR associated with MS between men and women; we had previously noted that the risk differs depending on the combination of criteria.[10] The criteria are also distributed differently when data are obtained from patients with CVD,[25] a fact which gives added interest to data obtained from the general population.

We also observed differences in the prevalence of MS between autonomous communities, with the Chartered Community of Navarre, Catalonia, and the Community of Madrid having the lowest rates, and the Canary Islands and Balearic Islands having the highest rates. A further difference was that women with MS had different levels of exposure to social factors (lower levels of education and fewer smokers) than those without MS, a pattern which was not observed in males. This may be an effect of age, as women with MS were almost a decade older than those without MS, while in men the age difference was only 4 years. Lower levels of education negatively affect lifestyle and this been previously associated with MS in other populations.[13] The fact that women with MS were older likely explains in part why they were less educated and there were fewer smokers, as social inequalities affecting women were more marked in older generations; in other populations, social class has proved a better predictor of MS in women than in men.[26]

Criticism of MS has mainly focused on its prognostic value, with some authors questioning whether its ability to predict DM and CVD is any greater than that of its individual components.[2,27–30] However, a recent study[31] with hundreds of thousands of patients concluded that MS was associated with a 2-fold increase in risk of CVD and a 1.5 times increase in risk of all-cause mortality. The authors of that study also showed that even when DM was excluded from the diagnostic criteria, MPMS was still associated with an increased risk of CVD. The wisest course may therefore be to accept that, even if individual MS criteria prove to be better predictors of DM or CVD, MS helps to identify individuals with a high CR which would not be detected if the diagnosis of MS was not taken into account. For that reason MPMS may be clinically relevant, because it defines individuals at high risk for DM or CVD while simultaneously reducing the population requiring primary prevention. Experts at the WHO[6] believe that future efforts should focus on health policies aimed at preventing the syndrome and on the study of its pathophysiology. In this regard, a causal explanation for MS is currently being sought in terms of adipose tissue dysfunction[32]; the theory of lipotoxicity by ectopic accumulation of fat is also of particular interest.[33] The connection between MS and the early stages of renal failure, which could be involved in the pathophysiological mechanism originating the syndrome, is also justifiably receiving attention.[34,35]

Strengths and Limitations

The strengths of the DARIOS study have been described previously.[7] They include the use of data from 11 population-based studies conducted in the 21st century in 10 regions covering most (70%) of the Spanish population aged 35 to 74 years. Furthermore, samples were randomly selected, the participation rate was high, and the results were analyzed for agreement with a reference laboratory. We must add that this is the largest sample of individuals with MS studied in Spain to date and the first study to investigate the potential impact of using MPMS.

A possible limitation would be that the sampling frame used in some of the component studies did not ensure representativeness of the autonomous community in question. On the other hand, the total sample represents approximately 70% of the general adult population of Spain and the results of the DARIOS study were very similar to those of the 2006 National Health Survey, when compatible questions in the two investigations were examined.[7]

The main limitation of our study is the interpretation of the CR, as the cross-sectional design made it necessary to estimate CR using a function rather than direct measurements following participants over time. In addition, in one of the component studies (REGICOR) abdominal waist measurements were only available in a small proportion of participants (26%). Fortunately, one of the other studies included in DARIOS was also conducted in Catalonia (ARTPER) and provided sufficient information on that criterion for the region in question. Another possible limitation was that history of CVD was self-reported and therefore prone to error, particularly as regards the presence of angina.

CONCLUSIONS

Prevalence of MS in the adult population of Spain is over 30%. In those aged up to 55 years, it is more frequent in men but becomes more frequent in women in the group aged over 65 years. The highest prevalence was seen in the Canary Islands and the Balearic Islands. Applying the concept of MPMS reduces the prevalence rate to 24% and defines a younger population in which primary prevention of DM and CVD can be employed. Individuals with MS show a homogenous distribution of MS criteria, with high blood sugar and triglycerides being more common in men and low HDL-C and abdominal obesity more common in women.

In a population such as that of Spain, with a low overall CR, MS is associated with only moderately increased CR, in both sexes. Although women have a lower CR than men overall, they show a proportionally higher increase in CR associated with MS and MPMS.

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CONFLICTS OF INTEREST

None declared.

SUPPLEMENTARY MATERIAL

Supplementary material associated with this article can be found in the online version available at doi:10.1016/j.rec.2011.10.017.

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