

## Original article

## Lifestyle and cardiovascular mortality in menopausal women: a population-based cohort study

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## ABSTRACT

**Introduction and objectives:** There are models for cardiovascular risk prediction in the general population, but the prediction of risk in postmenopausal women has not been specifically studied. This study aimed to determine the association of lifestyle habits and chronic diseases with cardiovascular risk in menopausal women, as well as to build a risk scale.**Methods:** Retrospective population-based cohort study using data from the 2011 National Health Survey of Spain as a data source. Women  $\geq 50$  years were included. The characteristics that best defined the life habits of the study women were collected, as well as their health status and self-reported medical history at the time of the survey. Follow-up data on all-cause mortality were obtained from participants from 2011 to 2017.**Results:** A total of 5953 women  $\geq 50$  years of age were included, with a mean age of  $66.4 \pm 11.4$  years. The incidence of cardiovascular mortality in the follow-up period was 4%. Vegetable consumption less than 1 time/week (HR, 1.758), smoking (HR, 1.816) or excess hours of sleep ( $\geq 9$  h/day, HR, 1.809), or to have main daily activity sitting most of the time (HR, 2.757) were related to cardiovascular mortality. The predictive model presents an honest C-index in test sample of 0.8407 (95%CI, 0.8025-0.8789).**Conclusions:** Life habits such as the consumption of vegetables, daily main activity, sleeping hours or smoking are risk factors for cardiovascular mortality of great relevance among menopausal women. A simple 6-year self-reported risk scale with high predictive capacity is provided.

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**Hábitos de vida y mortalidad cardiovascular de las mujeres menopáusicas: estudio de cohortes de base poblacional**

## RESUMEN

**Introducción y objetivos:** Existen modelos de predicción de riesgo cardiovascular en población general, pero no se ha estudiado de modo específico la predicción del riesgo de las mujeres posmenopáusicas. El objetivo de este estudio es conocer los hábitos de vida y las enfermedades crónicas asociados con mayor riesgo cardiovascular en mujeres menopáusicas, así como construir una escala de riesgo.**Métodos:** Estudio de cohortes retrospectivo de base poblacional cuya fuente de datos es la Encuesta Nacional de Salud de España de 2011. Se incluyó a mujeres de edad  $\geq 50$  años. Se recogieron las características que mejor definían los hábitos de vida de las mujeres del estudio, así como su estado de salud y los antecedentes médicos declarados por ellas en el momento de la encuesta. Se realizó seguimiento de la mortalidad de las mujeres del estudio desde 2011 hasta 2017.**Resultados:** Se incluyó a 5.953 mujeres con una media de edad de  $66,4 \pm 11,4$  años. La incidencia de mortalidad cardiovascular en el periodo de seguimiento fue del 4%. Se relacionaron con la mortalidad cardiovascular el consumo de verduras menor de 1 vez/semana (HR = 1,758), el tabaquismo (HR = 1,816) el exceso de horas de sueño ( $\geq 9$  h/día, HR = 1,809) o tener actividad principal diaria sentada la mayor parte del tiempo (HR = 2,757). El modelo predictivo presenta un estadístico C «sincero» en muestra de prueba de 0,8407 (IC95%, 0,8025-0,8789).

## Palabras clave:

Factores de riesgo cardiovascular

Posmenopausia

Mujeres

Mortalidad

Enfermedad cardiovascular

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**Conclusiones:** Hábitos de vida como el consumo de verduras, la actividad principal diaria, las horas de sueño o el tabaquismo son factores de riesgo de mortalidad cardiovascular de gran relevancia entre las mujeres menopáusicas. Se aporta una sencilla escala de riesgo autorreferida a 6 años con elevada capacidad predictiva.

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## Abbreviations

BMI: body mass index  
 CVD: cardiovascular disease  
 ENSE11: 2011 Spanish National Health Survey  
 HR: hazard ratio

## INTRODUCTION

Cardiovascular disease (CVD) is the leading cause of morbidity and mortality worldwide.<sup>1</sup> Guidelines exist for the primary prevention of CVD and their aim is to establish recommendations to reduce risk,<sup>2</sup> but there are considerable differences between men and women.<sup>3</sup> According to data from the United States for the period 2013 to 2016, premenopausal women had lower rates of CVD than men of the same age, whereas postmenopausal women had higher rates.<sup>4</sup> The difference was even greater for women in early menopause.<sup>5</sup> Differences in health care are also a cause for concern. Because CVD presents differently in women, it is often diagnosed and treated later than in men, increasing the risk of poor outcomes.<sup>6</sup>

Many CV risk prediction models exist for the general population.<sup>7</sup> While most do not account for the differential characteristics of women, a number of models in the United States have included female-specific risk factors.<sup>8,9</sup>

It has been shown that women with diabetes have a 58% greater risk of coronary heart disease and a 13% greater risk of all-cause mortality than men with the same condition.<sup>10</sup> Similarly, hyperlipidemia appears to be associated with an increased CVD risk in postmenopausal women.<sup>11</sup> No clear associations, however, have been identified for other classic risk factors such as smoking and alcohol consumption in this population.<sup>12</sup> Obesity<sup>13</sup> and sedentary behavior may increase the risk of CVD and hospitalization for heart failure in women after menopause.<sup>14</sup>

The aim of this study was to determine the influence of lifestyle habits and chronic disease on increased CV risk in a representative sample of women of menopausal age from a national health survey in Spain and to use our findings to build an easy-to-apply risk scale.

## METHODS

We performed a population-based retrospective observational cohort study using data from the 2011 National Spanish Health Survey (ENSE11) conducted by the National Statistics Institute (INE) between July 2011 and June 2012. This survey is representative of all residents aged over 18 years in Spain and the sample was obtained using a complex stratified 3-stage design. The study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the Office of Responsible Research at *Universidad Miguel Hernández* in Elche, Alicante.

We included women aged 50 years and older and excluded those with missing data for any of the study variables. Information was collected on sociodemographic variables, the population characteristics that best defined the lifestyle habits of the women included,

self-reported health status and medical history at the time of the survey, and mortality data for a 6-year follow-up period (2011–2017). Mortality data were provided by the INE, which used probabilistic record linkage to match data from the ENSE11 to causes of death from the national death registry. We distinguished between mortality due to CVD (deaths due to diseases of the circulatory system [codes 100–199 in the 10th revision of the International Classification of Diseases]) and mortality due to other causes.

The following exposure variables were extracted from the ENSE11:

- Sociodemographic variables: age, place of residence (autonomous community), social class based on occupation of reference person,<sup>15</sup> country of birth, civil status, level of education, and net monthly household income.
- Lifestyle variables: smoking, exposure to environmental smoke, alcohol consumption, hours of daily sleep, type of physical activity in main daily activity, frequency of physical activity in leisure time, dental hygiene, and consumption of fruit, vegetables, pulses, dairy products, sweet products, and fast food.
- Health status: body mass index (BMI), use of a hearing aid, chronic or long-term diseases, current or past history of hypertension, myocardial infarction, other heart diseases, varicose veins, osteoarthritis, chronic neck pain, chronic lower back pain, allergies, asthma, chronic obstructive pulmonary disease, diabetes mellitus, stomach ulcer, urinary incontinence, high cholesterol, cataracts, chronic skin diseases, constipation, cirrhosis, migraine, hemorrhoids, osteoporosis, thyroid problems, stroke, malignant tumor, chronic depression, chronic anxiety, permanent injury due to an accident, or mental health.
- Self-reported health and health-related quality of life: self-perceived health in the past 12 months, self-rated health on the 5-level EQ-5D (EQ-5D-5L) visual analog scale (VAS), and limitations in activities of daily living due to health problems in the past 6 months or longer.
- Use of health services: admission to hospital in the past 12 months, admission to a day hospital in the past 12 months, emergency care in the past 12 months, primary care visit in the past month, specialist consultation in the past month, physical therapy in the past year, psychology consultation in the past year, radiography in the past year, computed tomography in the past year, ultrasound in the past year, magnetic resonance imaging in the past year, and vaccination in the last flu vaccination campaign.

The items within each category are shown in the [methods section of the supplementary data](#).

## Statistical analysis

Frequencies of all qualitative variables were calculated for the descriptive analysis. Factors associated with CV mortality were analyzed using contingency tables and the chi-square test. To estimate the magnitude of CV risk over 6 years, we built multivariate Cox models that adjusted for competing risks between CV mortality and mortality due to other causes using the approach of Putter et al.<sup>16</sup>

applied by Moore.<sup>17</sup> Hazard ratios (HRs) with 95% confidence intervals (95%CI) were calculated. The most parsimonious model was selected using the Akaike Information Criterion with forward stepwise selection. The proportional hazards assumption of the model was tested, as was goodness of fit using the likelihood ratio test (LRT). The predictive performance of the model was tested using the C index and 95%CI. The model was built using a random sample of 70% of the original sample and validated using the remaining 30%. The results of the optimal model were used to build a 6-year CV mortality risk scale following the approach described by Sullivan et al.<sup>18</sup> To obtain a representative sample of the Spanish population within the complex sampling approach, we applied the raising factor of the sample divided by its mean as a weighting factor; this method provides weights centered around the mean.<sup>19</sup> The analyses were performed in SPSS v.21

## RESULTS

Of the 21 007 individuals surveyed in the ENSE11, 6223 were women older than 50 years; 270 (4.3%) were excluded due to missing values, leaving 5953 for analysis. Their mean age was  $66.4 \pm 11.4$  years (range, 50–103 years). The number and percentage of women in each of the lifestyle and chronic CVD-related disease categories are shown in table 1, together with cumulative rates for CV mortality and mortality due to other causes. The estimated rate calculated for the 6 years of follow-up was 4% (n = 239) for CV mortality and 7% (n = 419) for mortality due to other causes. Mean age at death was  $83.5 \pm 8.6$  years for women who died of CVD and  $78.6 \pm 10.8$  years for those who died of another cause. Cumulative CV mortality and mortality due to other causes according to socio-demographic characteristics, other chronic diseases, self-rated health

**Table 1**  
Cumulative incidence of cardiovascular mortality and morbidity due to other causes according to lifestyle habits and chronic disease

	Total		Alive		Died of cardiovascular disease		Died of another cause		P
	No.	%	No.	%	No.	%	No.	%	
<i>Body mass index</i>									< .001
Normal	1983	33.3	1814	91.5	54	2.7	115	5.8	
Overweight	1874	31.5	1713	91.4	56	3.0	105	5.6	
Obesity	1189	20.0	1060	89.1	49	4.1	80	6.8	
DK/DA	907	15.2	709	78.1	80	8.8	118	13.0	
<i>Smoking</i>									< .001
Never	4497	75.5	3897	86.6	227	5.0	374	8.3	
Exsmoker	693	11.6	663	95.7	9	1.3	21	3.0	
Smoker	763	12.8	735	96.5	3	0.4	24	3.1	
<i>Exposure to environmental smoke</i>									< .001
Never	5033	84.5	4426	87.9	220	4.4	387	7.7	
< 1 h/d	370	6.2	346	93.4	10	2.6	15	3.9	
> 1 h/d	550	9.2	523	95.2	9	1.7	17	3.1	
<i>Alcohol</i>									< .001
Does not drink	4231	71.1	3663	86.6	205	4.9	363	8.6	
Mean daily intake over a wk $\leq$ 20 g	1549	26.0	1464	94.5	32	2.1	53	3.4	
Mean daily intake over a wk $\leq$ 20 g	173	2.9	169	97.4	1	0.8	3	1.9	
<i>Hours of sleep</i>									< .001
> 9 h/d	386	6.5	247	64.0	64	16.6	75	19.4	
7–9 h/d	3619	60.8	3324	91.8	105	2.9	191	5.3	
< 7 h/d	1948	32.7	1725	88.6	70	3.6	153	7.8	
<i>Main daily activity</i>									< .001
Sitting most of the day	2339	39.3	1815	77.6	200	8.5	323	13.8	
Standing most of the day	3124	52.5	3002	96.1	36	1.2	86	2.7	
Walking-tasks involving exertion	490	8.2	478	97.6	2	0.5	9	1.9	
<i>Physical activity during free time</i>									< .001
Sedentary behavior	3025	50.8	2498	82.6	208	6.9	319	10.5	
Occasional activity	2358	39.6	2244	95.2	29	1.2	85	3.6	
Frequent activity	306	5.1	298	97.5	2	0.6	6	1.9	
Sports training	265	4.4	256	96.6	1	0.3	8	3.1	
<i>Fruit consumption</i>									.229
Daily	4591	77.1	4104	89.4	173	3.8	314	6.8	
> 3 times/wk	772	13.0	678	87.8	32	4.2	62	8.1	
1–2 times/wk	370	6.2	325	87.9	19	5.0	26	7.1	
< 1 time/wk	219	3.7	188	86.0	15	6.7	16	7.3	
<i>Consumption of vegetables</i>									< .001
Daily	3366	56.5	3037	90.2	119	3.5	210	6.2	

**Table 1** (Continued)

Cumulative incidence of cardiovascular mortality and morbidity due to other causes according to lifestyle habits and chronic disease

	Total		Alive		Died of cardiovascular disease		Died of another cause		P
	No.	%	No.	%	No.	%	No.	%	
> 3 times/wk	1906	32.0	1687	88.5	79	4.1	141	7.4	
1-2 times/wk	516	8.7	448	86.7	26	5.0	43	8.3	
< 1 time/wk	164	2.8	124	75.5	15	9.1	25	15.4	
<i>Consumption of pulses</i>									.004
Daily	91	1.5	85	92.6	1	0.7	6	6.6	
> 3 times/wk	1383	23.2	1213	87.7	62	4.5	108	7.8	
1-2 times/wk	3608	60.6	3240	89.8	130	3.6	239	6.6	
< 1 time/wk	698	11.7	620	88.8	31	4.4	47	6.7	
Never/almost never	172	2.9	138	80.2	15	8.8	19	11.0	
<i>Consumption of dairy products</i>									.336
Daily	5204	87.4	4630	89.0	208	4.0	365	7.0	
> 3 times/wk	340	5.7	304	89.4	17	4.9	20	5.8	
1-2 times/wk	159	2.7	147	92.4	3	1.6	10	6.0	
< 1 time/wk	97	1.6	86	89.0	2	2.5	8	8.6	
Never/almost never	154	2.6	128	83.6	9	6.0	16	10.4	
<i>Consumption of sweet products</i>									.009
Daily	1607	27.0	1395	86.8	78	4.8	134	8.3	
> 3 times/wk	747	12.6	662	88.6	31	4.1	54	7.3	
1-2 times/wk	942	15.8	854	90.7	31	3.3	57	6.0	
< 1 time/wk	1070	18.0	982	91.8	30	2.8	57	5.4	
Never/almost never	1586	26.6	1402	88.4	69	4.3	116	7.3	
<i>Consumption of fast food</i>									<.001
> 3 times/wk	76	1.3	68	88.7	3	3.3	6	8.0	
1-2 times/wk	357	6.0	330	92.3	6	1.6	22	6.1	
< 1 time/wk	904	15.2	855	94.6	14	1.5	35	3.9	
Never/almost never	4615	77.5	4042	87.6	217	4.7	355	7.7	
<i>Dental hygiene</i>									<.001
≥ 3 times/d	2201	37.0	2067	93.9	51	2.3	83	3.7	
2 times/d	1985	33.3	1811	91.2	57	2.9	117	5.9	
1 time/d	1207	20.3	1030	85.3	63	5.3	114	9.4	
Never/occasionally	561	9.4	388	69.2	67	12.0	105	18.7	
<i>Chronic disease</i>									<.001
No	2016	33.9	1901	94.3	38	1.9	77	3.8	
Yes	3937	66.1	3395	86.2	201	5.1	342	8.7	
<i>Hypertension</i>									<.001
No	3438	57.7	3167	92.1	78	2.3	193	5.6	
Yes	2515	42.3	2129	84.6	161	6.4	225	9.0	
<i>Acute myocardial infarction</i>									<.001
No	5804	97.5	5194	89.5	218	3.8	392	6.8	
Yes	149	2.5	102	68.2	21	14.0	27	17.8	
<i>Other heart diseases</i>									<.001
No	5269	88.5	4794	91.0	147	2.8	328	6.2	
Yes	684	11.5	502	73.3	92	13.5	90	13.2	
<i>Diabetes mellitus</i>									<.001
No	5110	85.8	4640	90.8	162	3.2	308	6.0	
Yes	843	14.2	656	77.9	76	9.1	110	13.1	
<i>High cholesterol</i>									.070
No	3937	66.1	3483	88.5	157	4.0	298	7.6	
Yes	2016	33.9	1813	89.9	82	4.1	120	6.0	
<i>Stroke</i>									<.001
No	5835	98.0	5227	89.6	215	3.7	393	6.7	
Yes	118	2.0	68	58.0	24	20.4	25	21.5	

DK/DA, didn't know/didn't answer.

and quality of life, and use of health care services are shown in [table 1 of the supplementary data](#). The mean EQ-5D-5L VAS score for self-rated health was  $67.5 \pm 20.9$  ( $50.3 \pm 21.9$ ) for women who died of CVD and  $52.2 \pm 23.0$  for those who died of another cause.

The results of the multivariate Cox model for CV mortality adjusted for competing causes of death and all the study variables analyzed are shown in [table 2](#). The model was built using a random sample of 4204 women (71%) and tested in the remaining 1749 (29%). The HRs for CV mortality are shown for each item within the predictor categories. Sitting during most of the day vs walking around and performing tasks requiring exertion in the person's main daily activity was the strongest predictor of CV mortality (HR = 2.757). This was followed by active smoking (HR = 1.816) vs having never smoked, sleeping for more than 9 hours a day (HR = 1.809) vs 7 to 9 hours, eating vegetables less than once a week (HR = 1.758) vs every day, and having been admitted to hospital in the past year (HR = 1.700). The only chronic diseases that independently predicted CV mortality were diabetes mellitus (HR = 1.522) and high cholesterol. BMI did not have independent

predictive power in the presence of the other factors. As seen in the last row of [table 2](#), there was a significant interaction between age and mortality due to other causes, such that the HR represents the difference in the effect of age on CV mortality and mortality due to other causes. In brief, the risk of mortality due to other causes was 0.955 times that of CV mortality. In other words, age contributed to a slightly increased risk of CV mortality compared with mortality due to other causes. The model fit the data well (LRT = 1072.6;  $P < .001$ ), met the proportional hazards assumption ( $P = .257$ ), and showed high predictive capacity in the validation sample, with a C index of 0.8407 (95%CI, 0.8025–0.8789).

The results of the multivariate model were used to assign a score to each risk factor and build a CV risk scale for women based on their lifestyle habits and the presence of chronic diseases ([table 3](#)). BMI and high cholesterol levels were not included as they did not have independent predictive power in the multivariate analysis. The sum of scores for each predictor indicates the probability of CV mortality over 6 years ([table 4](#)). For example, an 85-year-old woman (5 points) who scored 80 on the EQ-5D-5L VAS

**Table 2**

Multivariate Cox model for cardiovascular mortality with adjustment for competing risks from other causes of death

	$\beta$	SE	HR (95%CI)	P
Age, y	0.131	0.011	1.140 (1.116–1.165)	< .001
EQ-5D-VAS	-0.012	0.003	0.988 (0.982–0.993)	< .001
<i>Body mass index</i>				
Normal	0		1	
Overweight	-0.177	0.162	0.837 (0.61–1.15)	.275
Obesity	0.011	0.174	1.011 (0.719–1.421)	.951
DK/DA	0.097	0.149	1.102 (0.823–1.475)	.514
<i>Smoking</i>				
Never	0		1	
Exsmoker	0.272	0.275	1.313 (0.766–2.251)	.321
Smoker	0.597	0.280	1.816 (1.049–3.145)	.033
<i>Hours of sleep</i>				
7–9 h/d	0		1	
> 9 h/d	0.593	0.157	1.809 (1.33–2.461)	< .001
< 7 h/d	0.235	0.121	1.265 (0.998–1.604)	.053
<i>Main daily activity</i>				
Walking around-tasks involving exertion	0		1	
Standing during most of the day	0.280	0.458	1.323 (0.539–3.245)	.542
Sitting during most of the day	1.014	0.467	2.757 (1.104–6.885)	.030
<i>Vegetable consumption</i>				
Daily	0		1	
> 3 times/wk	0.074	0.125	1.077 (0.843–1.376)	.551
1–2 times/wk	0.073	0.186	1.076 (0.747–1.549)	.694
< 1 time/wk	0.564	0.220	1.758 (1.143–2.707)	.010
<i>Diabetes mellitus</i>				
Yes	0.420	0.126	1.522 (1.189–1.949)	.001
<i>High cholesterol</i>				
Yes	-0.315	0.114	0.730 (0.584–0.912)	.006
<i>Hospital admission in past year</i>				
Yes	0.531	0.140	1.700 (1.292–2.237)	< .001
Age* other causes	-0.046	0.012	0.955 (0.933–0.978)	< .001

95%CI, 95% confidence interval; DK/DA, didn't know/didn't answer; EQ-5D-VAS, 5-level EQ-5D visual analog scale; HR, hazard ratio; SE, standard error.

Training sample, n = 4204; cardiovascular deaths, n = 177; deaths due to another cause, n = 348; likelihood ratio test ( $\chi^2 = 1072.6$ ;  $P < .001$ ); C index = 0.8656 (95%CI, 0.8472–0.8840); proportional hazards test,  $P = .257$ .

Validation in test sample (n = 1749); "honest" C index = 0.8407 (95%CI, 0.8025–0.8789).

\* Interaction with mortality due to other causes.

(0 points), smoked (1 point), slept an average of 8 hours a day (0 points), spent most of her day sitting (2 points), ate vegetables 3 times a week (0 points), did not have diabetes (0 points), and had been admitted to hospital once in the past year (1 point) would have a 33% risk of dying of CVD in the next 6 years (total score, 9 points). The curve showing the risk of CV mortality according to total score is shown in figure 1.

## DISCUSSION

We have shown that lifestyle habits are closely linked to CV mortality in women of menopausal age. Vegetable consumption, physical activity, smoking, and number of hours spent sleeping carried as much or more weight than chronic diseases or classic CV risk factors. We used our findings to design a simple 6-year CV risk scale based on self-reported data that had high predictive capacity.

### Prevalence of CV risk factors

CV risk factors were common in the women studied: 42% had hypertension, 14% diabetes, and 34% high cholesterol. This

**Table 3**  
Risk scale for each category of predictor variables from the multivariate model

Risk factor	Category	Score
Age, y	50-54	-2
	55-59	-1
	60-64	0
	65-69	1
	70-74	2
	75-79	3
	80-84	4
	85-89	5
	90-94	6
	95-99	7
EQ-5D-VAS (0-100)	0-24	1
	25-49	0
	50-74	0
	75-100	0
Smoking	Never smoked	0
	Exsmoker	0
	Smoker	1
Sleep duration	≤ 9 h/d	0
	> 9 h/d	1
Main daily activity	Walking-tasks involving exertion	0
	Standing for most of the day	0
	Sitting for most of the day	2
Vegetable consumption	Daily	0
	≥ 3 times/wk	0
	1-2 times/wk	0
	< 1 time/wk	1
Diabetes	No	0
	Yes	1
Hospital admission in past year	No	0
	Yes	1

EQ-5D-VAS, 5-level EQ-5D visual analog scale.

**Table 4**

Probability of cardiovascular death over 6 years according to risk scale

Sum of points	Estimated risk (%)
≤ 2	≤ 0.4
1	0.5
2	0.9
3	0.8
4	1.5
5	2.9
6	5.4
7	10.2
8	18.8
9	33.0
10	53.7
11	77.3
≥ 12	> 94.0

indicates that there is much room for improvement in interventions aiming to promote heart-healthy diets, physical exercise, and avoidance of smoking or excessive alcohol intake. The proportion of women leading a sedentary life—51%—is similar to rates described in countries with different geographic, sociocultural, and economic backgrounds, such as Bangladesh (58%),<sup>20</sup> India (55%),<sup>21</sup> and Cameroon (51.9%).<sup>22</sup>

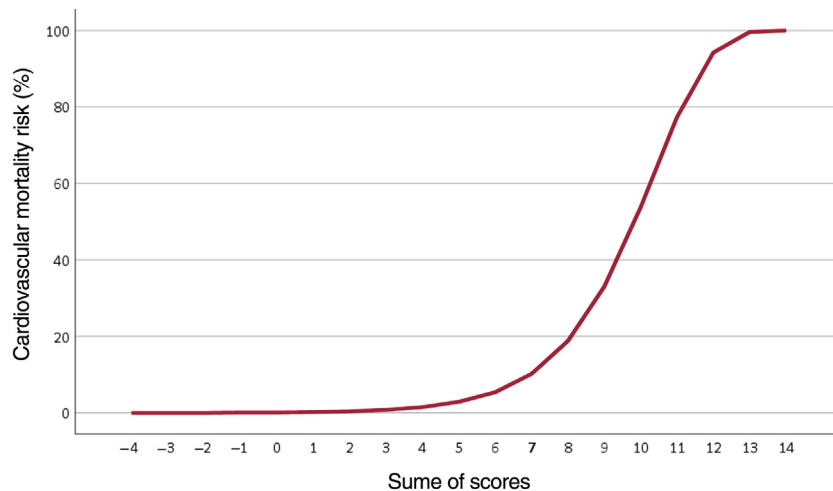
### Obesity

Numerous studies have analyzed the association between weight and CVD in postmenopausal women. It has been postulated that abdominal, not general, obesity is linked to insulin dependence and onset of diabetes and CVD,<sup>23</sup> and one of the predisposing factors for centrally distributed obesity is early postmenopause. The combination of age, menopause, and abdominal obesity has been linked to the accumulation of classic CV risk factors such as hypertension, dyslipidemia, and diabetes.<sup>13</sup> As in other settings such as heart failure, stroke, and atrial fibrillation, obesity defined by BMI exerts a protective effect against CVD.<sup>24,25</sup>

### Diet

Dietary phytoestrogens, which are diphenolic components present at high levels in fruit and vegetables, have been shown to counter the antiestrogenic effects of postmenopause.<sup>26</sup> Accordingly, they may be especially beneficial in populations such as ours. Basic research has identified a number of possible mechanisms underlying the beneficial effects of phytoestrogens, namely, affinity for estrogen receptors, antioxidant properties, and antiangiogenic and antiproliferative effects.<sup>27</sup> Consumption of plant-based rather than animal-based protein has been shown to reduce low-density lipoprotein cholesterol and triglycerides.<sup>28</sup> Unlike other strategies for reducing CV risk in postmenopausal women, eating vegetables has been shown to simultaneously reduce the risk of breast cancer.<sup>27</sup> Vegetable consumption in our series was the strongest modifiable predictor of CV mortality and mortality due to other causes.





**Figure 1.** Cumulative risk curve according to risk prediction scale scores.

### Physical activity

Physical activity has been shown to reduce CV risk in both the general population and postmenopausal women.<sup>29</sup> Indeed, high levels of inactivity are thought to be one of the reasons why postmenopausal women have a higher CV risk than men.<sup>30</sup> We were able to distinguish between women who engaged in physical activity for leisure and those whose main daily activity involved being physically active (regardless of whether or not this activity was considered to be work-related). Being active as part of one's main daily activity was closely associated with a lower risk of CV mortality, where leisure-time physical activity had no predictive capacity in the presence of other factors.

Although numerous studies have shown that nonoccupational physical activity reduces CV risk, very few studies have adjusted for physical activity performed as part of the person's main daily activity. We believe that this novel distinction is important, as work-related or similar physical activity occupies many more hours—and years—than leisure-time physical activity, which is typically performed for 30 to 120 minutes a day 2 to 5 days a week. In our sample, the number of hours spent sitting or lying down was directly associated with CVD, supporting previous findings.<sup>14</sup> Many of the studies showing the benefits of physical activity programs on CV risk in women have been conducted in sedentary, obese women,<sup>20</sup> but the effect might be diluted in women who are very physically active in their daily routines. Cross-sectional studies analyzing the effects of physical activity in postmenopausal women have shown an inverse correlation between CVD risk and physical activity, with greater reductions observed with increasing activity.<sup>20</sup> Leisure-time physical activity is obviously very important for sedentary women, but its effects are diluted in women whose daily routines involve being physically active.

### Hours of sleep

Previous research has shown an association between CVD and excessive or deficient sleep,<sup>31</sup> but none of the studies have specifically analyzed postmenopausal women. Although the causal associations between sleep duration and CVD are unclear, there are indications that genetic predisposition<sup>31</sup> and concomitant risk

factors such as dyslipidemia and insufficient physical activity<sup>32</sup> may contribute to an increased CV risk. Predisposition to adverse coronary events has been shown in this setting.<sup>33</sup>

### Nonsignificant classic CV risk factors in our population

High cholesterol, a known CV risk factor, exerted a protective effect in our cohort. We believe there are several reasons for this. Because our data were taken from a survey on lifestyle habits, we did not have access to lipid profiles, but a considerable proportion of the women diagnosed with high cholesterol were probably on treatment with statins, which have a strong protective role in CVD. There is also a close association between cholesterol levels and fruit and vegetable intake and physical activity, with basic research indicating that higher fruit and vegetable consumption reduces atherosclerosis linked to serum cholesterol levels.<sup>34</sup> Because our results are based on self-reported data, the presence of hypercholesterolemia may be underestimated.

### Lifestyle CV risk scale

CV risk scales have a dual purpose: to identify people with increased CV risk and to raise awareness among patients and health care professionals of the importance of adhering to treatments and encouraging action in this regard. Although current scales adjust for differences between men and women, the adjustments are exclusively quantitative in nature. Our risk scale, by contrast, is based on data from women of menopausal age, providing an easy-to-use scale directly applicable to postmenopausal women. A score of 6 points or more indicates a 5% increased risk in CV mortality but, as shown in figure 1, risk increases sharply after a score of 7. Age adds up to 2 points to the risk of premature CV death (before the age of 74 years). To maintain this risk under 5% thus, it is sufficient to refrain from smoking, take some physical activity every day, and eat plenty of vegetables.

### Limitations and strengths

Our study has some limitations. Because of its retrospective, observational design, we cannot infer any causal relationships

or rule out the presence of selection and exclusion biases. Although we controlled for confounders in our multivariate analysis, we cannot fully rule out the possibility of confounding. Likewise, some predictors of CV risk may be missing from our model. Our study also has some strengths, in particular the complex sampling design used, which provided representative estimates from a cohort of women older than 50 years living in Spain in 2011.

## CONCLUSIONS

CV risk in women of menopausal age is significantly influenced by lifestyle habits. Factors such as vegetable consumption and physical activity are very important in this population. Other factors, however, such as high cholesterol and obesity, which are strong predictors in men, do not appear to have predictive value in postmenopausal women.

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## AUTHORS' CONTRIBUTIONS

J.A. Quesada, V. Bertomeu-González, J.M. Ruiz-Nodar, A. López-Pineda, and F. Sánchez-Ferrer contributed to the study design. J.A. Quesada requested the data and performed the statistical analyses. J.A. Quesada, V. Bertomeu-González, J.M. Ruiz-Nodar, A. López-Pineda, and F. Sánchez-Ferrer contributed to the interpretation of data. J.A. Quesada, V. Bertomeu-González, J.M. Ruiz-Nodar, A. López-Pineda, and F. Sánchez-Ferrer contributed to writing the manuscript. All the authors approved the final version of this manuscript.

## CONFLICTS OF INTEREST

None.

### WHAT IS KNOWN ABOUT THE TOPIC?

- CVD is the leading cause of morbidity and mortality worldwide but there are marked differences between men and women. The prevalence of CV disease is lower in premenopausal women than in men of the same age but the opposite is true for postmenopausal women.
- Many CV risk prediction models exist for the general population, but no studies have specifically analyzed predictors in postmenopausal women.

### WHAT DOES THIS STUDY ADD?

- CV risk in postmenopausal age is significantly influenced by lifestyle habits. Vegetable consumption, physical activity, smoking, and number of hours spent sleeping carry as much or more weight than chronic diseases or classic CV risk factors. We have designed a simple 6-year CV risk scale based on self-reported data that has high predictive capacity.

## APPENDIX. SUPPLEMENTARY DATA

Supplementary data associated with this article can be found in the online version available, at <https://doi.org/10.1016/j.rec.2021.10.006>

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