

## ORIGINAL ARTICLES

### ISCHEMIC HEART DISEASE

# Trends in Mortality From Ischemic Heart Disease in 50 Spanish Provinces

Raquel Boix Martínez, Nuria Aragonés Sanz and M. José Medrano Albero

Centro Nacional de Epidemiología, Instituto de Salud Carlos III, Madrid, Spain,

**Introduction and objectives.** Ischemic heart disease is the leading cause of cardiovascular mortality and the second most frequent cause in women in Spain. It is responsible for 12% and 10%, respectively, of all-cause mortality. Our aim was to identify those provinces where recent trends differ significantly from the overall national pattern of decreasing rates in recent years, and where intervention is probably needed.

**Patients and method.** We report mortality trends due to ischemic heart disease for the periods 1988-1991 and 1994-1997 for each province in persons aged 35 to 64 years, and mortality trends in Spain in the last 19 years for all age groups. Data for ischemic heart disease mortality were obtained from files supplied by the Spanish National Institute for Statistics. Mortality rates in the two 4-year periods were compared with log-linear Poisson regression models to estimate trends. Age-adjusted and mortality hazard-rates are presented with 95% CI, and time trends and geographical variations are also reported.

**Results.** The highest rates were seen at Andalucía (south), Levante (east) and the oversea provinces (Balearic [Mediterranean] and Canary Islands [Atlantic]). There were considerable geographical differences in mortality rates. Time trends showed a decrease in men in 27 provinces and a decrease in women in 12 provinces. Overall mortality trends decreased in the last 19 years in Spain.

**Conclusions.** Although the general trend is toward a decrease, there are differences between provinces in Spain. The previously reported North-South gradient and regional discrepancies were confirmed.

**Key words:** *Epidemiology. Ischemic heart disease. Mortality.*

### Tendencias en la mortalidad por cardiopatía isquémica en 50 provincias españolas

**Introducción y objetivos.** A pesar de la tendencia decreciente de los últimos 25 años, la cardiopatía isquémica continúa siendo la primera causa de muerte en varones y la segunda en mujeres, con un 12 y un 10% de la mortalidad total, respectivamente. Nuestro objetivo es comprobar si, en el ámbito nacional, el descenso de la mortalidad se mantiene en periodos recientes y en cada una de las provincias, e identificar aquellas donde existen desviaciones significativas del patrón general que aconsejan realizar intervenciones prioritarias.

**Pacientes y método.** Se compara la mortalidad provincial por cardiopatía isquémica en dos cuatrienios (1994-1997 frente a 1988-1991) en la población de 35-64 años, así como la evolución de las tasas de mortalidad en España desde 1980 hasta 1998 para todos los grupos de edad, utilizando datos de defunciones del Instituto Nacional de Estadística. La comparación de la mortalidad entre ambos cuatrienios se ha realizado mediante modelos Poisson de regresión logarítmica lineales, obteniendo la razón de tasas ajustada por edad y sus intervalos de confianza del 95%.

**Resultados.** Las áreas que presentaron tasas de mortalidad superiores corresponden al sur, levante y regiones insulares. Para todos los grupos de edad, la tendencia en los últimos 19 años es ligeramente decreciente en todo el territorio nacional. Se produce un descenso estadísticamente significativo en 27 provincias entre los varones y en 12 provincias entre las mujeres. En gran parte del territorio, la mortalidad por cardiopatía isquémica no desciende significativamente.

**Conclusiones.** Aunque la tendencia general es decreciente, el descenso no es homogéneo, y se mantienen el patrón norte-sur y las desigualdades territoriales.

**Palabras clave:** *Epidemiología. Cardiopatía isquémica. Mortalidad.*

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Correspondence: Dra. R. Boix Martínez.  
Centro Nacional de Epidemiología. Instituto de Salud Carlos III.  
Sinesio Delgado, 6. 28029 Madrid. Spain.  
E-mail: [rboix@isciii.es](mailto:rboix@isciii.es)

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## INTRODUCTION

Ischemic heart disease continues to be the leading cause of death in adults in developed countries. In Spain, it is the leading cause of death in men and the second leading cause of death in women.<sup>1</sup> In 1998, 22 352 men and 17 090 women died from ischemic

## ABBREVIATIONS

MONICA: Monitoring trends and determinants of cardiovascular disease.  
 IBERICA: Identificación, búsqueda específica y registro de isquemia coronaria aguda.  
 PRIAMHO: Proyecto de Registro de Infarto Agudo de Miocardio Hospitalario.  
 ARIAM: Análisis retraso infarto agudo miocardio.  
 PREVESE: Prevención secundaria en España.

heart disease in Spain, representing 37.09% and 23.42% of cardiovascular mortality for men and women respectively, and 11.86 and 10.08%, respectively, of all-cause mortality.

In Spain, several population registers are used to monitor acute myocardial infarct (AMI), including the MONICA database in Catalonia<sup>2</sup> and the IBERICA database.<sup>3</sup> Using the IBERICA database, the incidence of AMI in the Spanish population aged 25 to 74 was estimated at 194 cases per 100 000 inhabitants/year for men and 38 cases per 100 000 inhabitants/year for women.<sup>4</sup>

These data indicate the importance of monitoring trends in ischemic heart disease and controlling its risk factors. Non-transmissible diseases, particularly cardiovascular disease, cancer and diabetes, are now considered a pandemic in the 21st century, and affect both developed and developing countries. The World Health Organization has promoted the monitoring of these diseases and their principal risk factors as part of an overall strategy for their prevention and control.

Monitoring trends over time and analyzing the geographic distribution of disease can be useful in detecting changes which suggest future risks for the population. Mortality data provide a good source of information as they are collected universally and their collection is highly standardized. For that reason, they allow comparisons to be made and are widely used to assess trends.

Spain has one of the lowest mortality rates from ischemic heart disease in the world, and the rate has been steadily decreasing over the past 25 years.<sup>1</sup> However, little is known about whether this general pattern also applies to different parts of Spain, nor whether there has been a trend towards a reduction in mortality from ischemic heart disease in individual provinces. The primary aim of the present study was to analyze mortality from ischemic heart disease in the population aged 35 to 64 years in different regions of Spain. A further aim was to identify regions in which significant deviations from the general trend might suggest a need for health care interventions.

## PATIENTS AND METHODS

Mortality data were obtained from individual registers supplied by the National Institute of Statistics. The diagnostic codes selected were 410-414, which correspond to ischemic heart disease in the Ninth Revision of the International Classification of Diseases.

### Statistical analysis

Mortality rates from ischemic heart disease in the population aged 35 to 64 were compared by province for two 4-year periods (1988-1991 and 1994-1997). The analysis took into account 3 age groups (35-44 years, 45-54 years and 55-64 years). For the two periods and the age groups mentioned, the denominators used were the populations in 1989 and 1995, respectively; these were calculated using interpolation methods based on the usual population statistics. Rates were compared using logarithmic linear regression models, in which it was assumed that the number of deaths in each age group and period showed a Poisson distribution.<sup>5</sup> In formulating the model, the population was introduced as an offset or constant; the dependent variable were deaths, which were allowed to vary in terms of age and period. Age and period were incorporated into the model as explanatory variables. Independent models were adjusted for each province and sex, and the variables age and time-period were introduced as factors. The model was designed to provide the age-adjusted rate ratio and 95% confidence intervals (CI), and to compare the two time periods in each province.

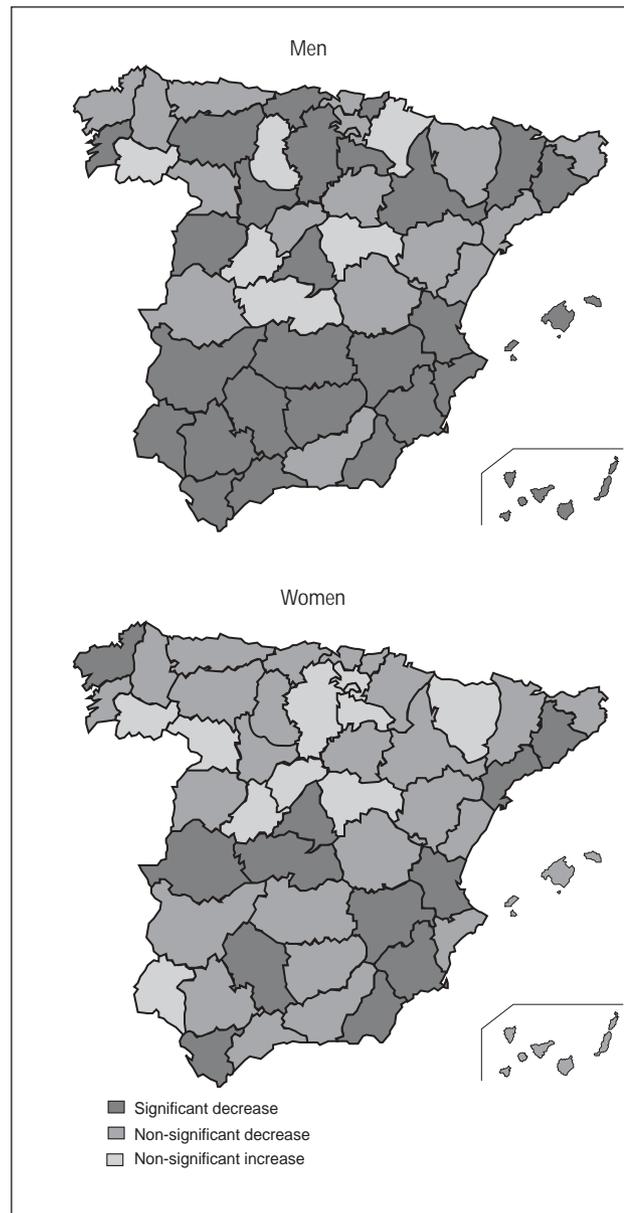
Adjusted mortality rates were calculated for each province for 1998 using the direct method with the standard European population, and 18 age groups for each sex. Adjusted mortality rates per 100 000 person-years are presented for each Spanish province in 1998. The evolution of mortality rates in Spain as a whole were analyzed for the period 1980-1998. The statistical significance of trends was obtained by adjusting simple linear regression using the S-Plus program. The percentage change between 1980 and 1998 was calculated using the formula  $(T80 - T98)/T80 \times 100$ , and the annual percent change was calculated using the formula recommended by López Abente et al.:<sup>6</sup>  $(\exp[(\ln(T80) - \ln(T98))/10] - 1) \times 100$ .

Lastly, Spanish data were compared with European data provided by the World Health Organization,<sup>7</sup> which include standardized mortality rates for the new standard world population for both sexes, all age groups, and per 100 000 person-years.

**TABLE 1. Provincial mortality from ischemic heart disease in Spain (1994-1997/1988-1991). Rate ratio in the population aged 35-64 years**

	Men		Women	
	Rate ratio	95% CI	Rate ratio	95% CI
Álava	0.917	0.708-1.188	1.080	0.505-2.309
Albacete	0.737	0.584-0.928	0.530	0.315-0.893
Alicante	0.852	0.774-0.938	0.860	0.700-1.057
Almería	0.727	0.601-0.880	0.658	0.452-0.958
Ávila	1.004	0.745-1.351	2.335*	1.171-4.660
Badajoz	0.701	0.611-0.804	0.867	0.648-1.161
Balearic Islands	0.710	0.623-0.810	0.747	0.550-1.015
Barcelona	0.808	0.762-0.857	0.806	0.704-0.924
Burgos	0.631	0.502-0.794	1.015	0.574-1.792
Cáceres	0.857	0.721-1.020	0.461	0.300-0.710
Cádiz	0.843	0.757-0.939	0.691	0.564-0.847
Castellón	0.865	0.729-1.026	0.802	0.539-1.194
Ciudad Real	0.822	0.682-0.991	0.693	0.461-1.041
Córdoba	0.818	0.707-0.945	0.677	0.503-0.912
A Coruña	0.899	0.807-1.002	0.758	0.581-0.987
Cuenca	0.816	0.597-1.115	0.615	0.339-1.114
Girona	0.893	0.751-1.061	0.938	0.637-1.382
Granada	0.918	0.800-1.053	0.908	0.683-1.206
Guadalajara	1.103	0.762-1.595	1.309	0.523-3.277
Guipúzcoa	0.789	0.683-0.913	0.910	0.632-1.311
Huelva	0.793	0.667-0.944	1.254	0.871-1.805
Huesca	0.785	0.588-1.047	1.061	0.565-1.992
Jaén	0.798	0.673-0.946	0.748	0.529-1.059
León	0.655	0.545-0.787	0.866	0.562-1.333
Lleida	0.777	0.621-0.972	0.907	0.557-1.479
La Rioja	0.762	0.592-0.981	1.046	0.552-1.983
Lugo	0.925	0.779-1.098	0.688	0.460-1.030
Madrid	0.816	0.768-0.867	0.800	0.688-0.930
Málaga	0.892	0.803-0.991	0.852	0.694-1.047
Murcia	0.742	0.656-0.838	0.729	0.571-0.930
Navarra	1.168	0.978-1.394	0.929	0.589-1.466
Orense	1.123	0.913-1.382	1.077	0.692-1.676
Asturias	0.909	0.820-1.008	0.842	0.655-1.081
Palencia	0.815	0.611-1.086	0.791	0.405-1.543
Las Palmas	0.976	0.866-1.101	0.823	0.659-1.028
Pontevedra	0.818	0.708-0.944	0.801	0.548-1.171
Salamanca	0.762	0.624-0.931	0.672	0.427-1.058
Santa Cruz de Tenerife	0.847	0.742-0.968	0.818	0.629-1.064
Cantabria	0.641	0.539-0.761	0.650	0.413-1.023
Segovia	0.937	0.641-1.369	1.550	0.657-3.659
Seville	0.825	0.755-0.901	0.839	0.697-1.009
Soria	0.756	0.475-1.203	0.561	0.231-1.361
Tarragona	0.890	0.744-1.063	0.656	0.441-0.975
Teruel	0.858	0.616-1.196	0.750	0.388-1.449
Toledo	1.099	0.917-1.319	0.704	0.499-0.992
Valencia	0.912	0.844-0.986	0.777	0.655-0.921
Valladolid	0.798	0.659-0.967	0.682	0.406-1.147
Vizcaya	0.987	0.872-1.118	0.847	0.619-1.159
Zamora	0.908	0.690-1.194	1.113	0.609-2.034
Zaragoza	0.793	0.697-0.902	0.889	0.654-1.208

\*The population in Ávila in the period and age groups studied decreased by 2120 and there were an additional 13 deaths. CI indicates confidence interval.



**Fig. 1.** Provincial mortality from ischemic heart disease in Spain (1994-1997/1988-1991). Rate ratio in the population aged 35-64 years.

## RESULTS

Table 1 compares provincial mortality rates from ischemic heart disease by sex in the Spanish population aged 35-64 using mortality rate ratios for the periods 1994-1997 and 1988-1991. In general, rates for both men and women were higher in 1988-1991 than in 1994-1997, as shown by the fact that the majority of the rate ratios were lower than 1. There was a statistically significant reduction in mortality among men in 27 provinces and among women in 12 provinces (Figure 1). In men, mortality rates increased between the two periods in only 5

**TABLE 2. Provincial mortality from ischemic heart disease in Spain (1998). Rates adjusted using the standard European population per 100 000 person-years**

	Men	Women
Álava	74.18	24.93
Albacete	92.04	39.33
Alicante	134.11	59.30
Almería	121.14	54.53
Ávila	82.61	38.26
Badajoz	112.53	50.78
Balearic Islands	108.58	42.50
Barcelona	98.05	42.18
Burgos	81.86	28.28
Cáceres	98.43	49.83
Cádiz	132.32	66.16
Castellón	125.37	55.44
Ciudad Real	87.64	44.43
Córdoba	110.39	53.00
A Coruña	97.90	41.77
Cuenca	71.49	35.66
Girona	83.99	37.95
Granada	123.81	66.01
Guadalajara	69.55	27.53
Guipúzcoa	90.41	34.25
Huelva	119.72	61.35
Huesca	74.87	28.30
Jaén	97.72	48.06
León	72.47	28.67
Lleida	79.21	42.67
La Rioja	85.81	28.83
Lugo	94.32	34.32
Madrid	84.82	34.18
Málaga	132.48	57.80
Murcia	105.31	53.99
Navarra	93.88	38.78
Orense	90.87	45.74
Asturias	118.96	51.71
Palencia	71.94	35.14
Las Palmas	164.42	75.30
Pontevedra	90.35	36.41
Salamanca	93.85	34.08
Santa Cruz de Tenerife	150.51	70.88
Cantabria	80.35	35.93
Segovia	67.69	33.60
Seville	143.68	75.82
Soria	66.85	38.98
Tarragona	82.19	36.73
Teruel	77.12	31.38
Toledo	90.35	40.70
Valencia	112.97	50.63
Valladolid	78.18	35.92
Vizcaya	90.77	36.02
Zamora	74.90	28.15
Zaragoza	98.30	39.90
Total	101.11	44.89

provinces, though the increases were not statistically significant. The largest rate ratios were observed in Navarra, Orense, Guadalajara, and Toledo. During

the second 4-year period (1994-1997), the population aged 35-64 in these provinces showed an excess risk of dying from ischemic heart disease of 17% in Navarra, 12% in Orense, and 10% in Guadalajara and Toledo compared with a similar population in the first 4-year period (1988-1991). The provinces of Burgos, Cantabria, and León showed the greatest reductions in mortality between the first and second periods, with a risk reduction of approximately 35% between the two periods. In women, the risk of dying from ischemic heart disease was higher in the second period in 10 provinces, although the increase in risk was only statistically significant in Ávila. Ávila is, however, a sparsely populated province and the absolute number of deaths is small, so this result should be treated with caution, due to the possible instability of the rates. An increase in the rate ratio was also observed in Segovia, Guadalajara, and Huelva, with an increased risk of dying from ischemic heart disease in these provinces of 55%, 31% and 25%, respectively.

Table 2 shows the provincial mortality rates from ischemic heart disease in Spain in 1998, presented as rates adjusted by the standard European population and per 100 000 person-years for all age-groups and both sexes. The overall rate for Spain was 101.11 in men and 44.89 in women. The regions with the highest mortality rates from ischemic heart disease were Andalusia, Asturias, the Balearic Islands, the Canary Islands, Extremadura, Murcia, and the Community of Valencia. In men, the highest rates were observed in the canary Islands, followed by Seville, Alicante, and Cádiz. The lowest rates were in Soria, Segovia, Guadalajara and Cuenca. In women, the highest rates were also found in the Canary Islands and in Seville, whilst the lowest rates were found in Álava, Guadalajara, Zamora, Burgos, and Huesca. There was a notable difference in mortality rates between provinces; in men, the province with the highest mortality had 2.42 times more mortality than the province with the lowest mortality and in women the difference was 3.04. There were also notable differences between the sexes in terms of mortality attributable to ischemic heart disease.

Table 3 and Figure 2 show the mortality rates from ischemic heart disease in Spain from 1980 to 1998 for all age-groups and both sexes, adjusted by the standard European population, and per 100 000 person-years. In the period in question, mortality from ischemic heart disease steadily decreased. In 1980, mortality in men was 115.07 cases per 100 000 person-years and in women it was 50.54; 18 years later the corresponding rates were 101.11 in men and 44.89 in women. The percent change over the period was 12% in men and 11% in women, with an annual percent change in men of 1.30% and 1.19% in women. The decrease was slightly more marked in

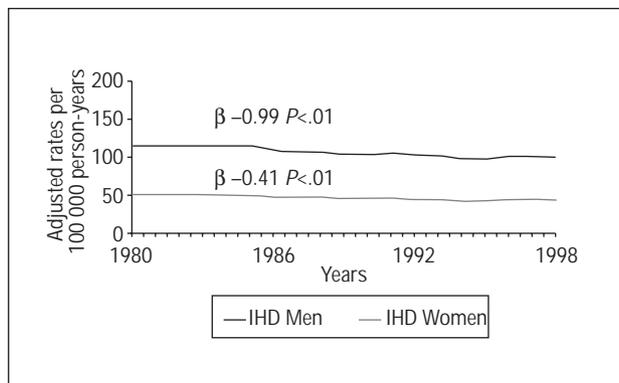
**TABLE 3. Mortality from ischemic heart disease in Spain (1980-1998). Rates adjusted using the standard European population per 100 000 person-years**

Year	Men	Women
1980	115.07	50.54
1981	114.27	50.84
1982	114.42	50.57
1983	114.35	51.90
1984	114.54	50.38
1985	115.15	49.94
1986	109.81	47.86
1987	108.09	47.91
1988	107.80	47.91
1989	104.63	46.58
1990	104.44	47.49
1991	105.86	47.41
1992	102.97	45.57
1993	102.85	45.59
1994	98.19	43.42
1995	98.33	44.04
1996	103.02	45.94
1997	101.00	45.14
1998	101.11	44.89

**TABLE 4. Mortality from ischemic heart disease in the European Union (1997-1999). Rates adjusted using the standard world population\*, per 100 000 person-years**

	Men	Women
Germany	150.9	76
Austria	153.9	77.7
Belgium	93.2	43.1
Denmark	148.9	72.9
Holland	111.7	47.9
Ireland	215.8	100.8
Luxembourg	103.6	44.6
United Kingdom	174.4	81.7
Spain	78.2	34.3
France	60.4	23.9
Greece	98.8	42.2
Italy	92.9	43.7
Portugal	78.9	38.5
Finland	213.8	94.9
Sweden	159.9	72

\*The standard world population used by the WHO in their latest statistics has changed with respect to earlier series.



**Fig. 2.** Mortality from ischemic heart disease in Spain (1980-1998). Rates adjusted using the standard European population per 100 000 person-years. IHD indicates ischemic heart disease.

men, although mortality rates in men were double those of women. In men, the trend estimated by the linear regression model corresponded to a beta coefficient of  $-0.99$  ( $P < .01$ ), with a beta coefficient in women of  $-0.41$  ( $P < .01$ ).

Table 4 shows the mortality from ischemic heart disease in other countries in the European Union, using adjusted rates for the standard world population. Rates are shown for 100 000 person-years and are provided for all age groups and both sexes. In both men and women, mortality rates from ischemic heart disease in Spain are amongst the lowest in Europe, with only France having a lower rate.

## DISCUSSION

The results of this study show that mortality from ischemic heart disease in Spain has decreased significantly over the period studied. Overall, for all age groups and for the country as a whole, the tendency over the last 19 years has been towards a slight but significant reduction in mortality. Specifically, in the 35-64-year-old age group studied here, the results show a significant reduction in mortality from ischemic heart disease in 27 provinces in men and in 12 provinces in women. Only Ávila showed a statistically significant increase in mortality from ischemic heart disease, but this result should be treated with caution due to the possible instability of the rates there.

Mortality from ischemic heart disease in men has not, however, decreased significantly in 23 provinces, and in women, in the majority of provinces ( $n=38$ ), mortality rates in 1994-1997 were not significantly lower than those observed 6 years earlier. In some cases, there is very little variation over the study period, a result which hints at a possible stabilization of mortality rates. In a small number of provinces, a non-statistically significant increase in mortality rates was observed, though this result needs to be confirmed over time. As a whole, our results indicate that the continuous reduction in mortality is not applicable to the whole of Spain, and that mortality is not decreasing in various regions.

The present study was carried out using official statistics. The MONICA study suggested that official statistics tend to exaggerate the trend towards reduced mortality in comparison with data obtained from

clinical records of patients in the population. While official statistics suggested that mortality in the MONICA population was decreasing at an annual rate of 4%, data for the same population from the MONICA study suggested a rate of reduction of 2.7% in men and 2.1% in women.<sup>2</sup> If the same bias existed in the present study, the result would be an even more notable stabilization of rates than that observed.

With respect to the geographic distribution of mortality, the results of the present study indicate that north-south differences still exist, with higher mortality rates in the south. Other important regional differences persist, and mortality rates are still higher in men than in women. Mortality, however, remains low in comparison to other developed countries. In general, the results of the present study are consistent with those from earlier studies<sup>8</sup>, including those using aggregated data from different regions<sup>9</sup> or municipalities,<sup>10</sup> as well as those which focused on specific regions such as Catalonia,<sup>11</sup> Andalusia,<sup>12</sup> the Community of Valencia,<sup>13</sup> Murcia<sup>14</sup> or the Canary Islands.<sup>15</sup>

Trends in mortality and the geographic distribution of cardiovascular disease can be explained by various factors including geographical differences, changes in the prevalence of cardiovascular risk factors,<sup>16-18</sup> differences in socioeconomic level, and differences in the quality of and access to health care. Factors such as the environment or tourism are have also been shown to be associated with differences in cardiovascular mortality. With regard to diet, the low consumption of fish and wine in Spain could explain the apparent contradiction between high levels of cardiovascular mortality and a low consumption of saturated fats in Mediterranean regions.<sup>19</sup> Results from the Four Provinces Study<sup>20</sup> show that children living in cities where mortality from ischemic heart disease is high have higher body mass indices, a higher caloric intake, and a higher consumption of cholesterol and sodium. Diabetes also shows a north-south pattern;<sup>10</sup> the highest mortality rates are observed in Extremadura, Andalusia, the Levant, and the Canary Islands. The IBERICA study<sup>3</sup> also showed a greater than 25% prevalence of diabetes in the Mediterranean regions studied, particularly Valencia and Murcia. Both of these regions have high vascular mortality rates.

The results of the MONICA study<sup>21</sup> also show, however, that the classic risk factors for cardiovascular mortality only explain 15% of mortality in women and 40% in men. The Eight Provinces Study<sup>22</sup> suggested that socioeconomic aspects and social inequalities might also affect mortality from ischemic heart disease, and the small areas Mortality Atlas provides evidence of an association between the distribution of cardiovascular mortality and patterns of illiteracy, unemployment and

overcrowding.<sup>10</sup> It has also been shown that socioeconomic level is the variable which best explains geographical variations in the prevalence of overweight and obesity in Spain.<sup>23</sup>

These factors are not directly susceptible to modification by the health care system, although they can be taken into account when assigning health care resources. The impact of existing inequalities of access to quality health care has been demonstrated by the MONICA study,<sup>2</sup> which showed that decreases in cardiovascular mortality are strongly associated with improvements in treatment for heart disease. The IBERICA study<sup>3</sup> showed that the hospital management of coronary patients varied across Spain, that there differences in the use of diagnostic and therapeutic resources, and differences in mortality. Studies which have investigated the hospital-based care of AMI patients, such as the PRIAMHO,<sup>24</sup> ARIAM,<sup>25</sup> and PREVESE II<sup>26</sup> studies, all showed that there are differences in access to health care and that aspects such as secondary prevention, or delays between the onset of AMI symptoms and health care, could be improved.

In terms of limitations, the present study suffers from the problems inherent in obtaining data from death certificates, although in the case of ischemic heart disease, death certificates in Spain have been shown to be of good quality.<sup>27</sup> As mentioned, biases revealed by the MONICA study are small and not significant when referring to a given period. They tend to magnify reductions in mortality when trends are analyzed. Some of the geographical differences found may be due to errors in classifying place of residence, an error which is particularly relevant in tourist areas, where mortality rates may be overestimated by the inclusion of the deaths of non-residents. Such an effect has been observed in tourist areas in the Canary Islands.<sup>15</sup> These limitations should be taken into account when interpreting the results of the study.

In conclusion, this study has shown that the reduction in mortality from ischemic heart disease observed in Spain as a whole is not homogenous across the country. The high prevalence of cardiovascular risk factors, together with geographical variations in the quality of health care resources and the access to these resources, provide ample opportunity for action and improvement. The results of the present study should be useful in prioritizing between geographical areas when deciding on where health care interventions should be focused.

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