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Original article

Trends in premature mortality due to ischemic heart disease in Spain from 1998 to 2018

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ABSTRACT

Introduction and objectives: Ischemic heart disease (IHD) is the leading cause of death and one of the leading causes of disability. The aim of this study was to analyze trends in premature mortality due to IHD in patients younger than 75 years in Spain from 1998 to 2018 by region.
Methods: Observational study of temporal trends in premature mortality due to IHD in Spain by region and sex from 1998 to 2018. The study population included resident citizens aged between 0 and 74 years. The data sources were the continuous population register and the mortality registry of the National Institute of Statistics. We calculated age-adjusted mortality rates and their average annual percent change estimated by Poisson models.
Results: During the study period, mortality rates due to IHD decreased, both in the country as a whole and by provinces (53% in men and 61% in women), with an average annual percent change of –3.92% and –5.07%, respectively. In the first year (1998), mortality was unequally distributed among provinces, with higher mortality in the south of Spain.
Conclusions: Premature mortality due to IHD significantly decreased in Spain during the study period in both sexes to roughly half of initial cases. This decrease was statistically significant in almost all regions. Interprovincial differences in mortality and their variation also decreased in recent years.

Tendencias de mortalidad prematura por cardiopatía isquémica en España durante el periodo 1998-2018

Palabras clave:
Cardiopatía isquémica
Mortalidad evitable
Mortalidad
Epidemiología
Población
Atención primaria

RESUMEN

Introducción y objetivos: La cardiopatía isquémica (CI) es la primera causa de mortalidad y una de las principales causas de discapacidad. El objetivo de este estudio es analizar las tendencias de la mortalidad prematura de menores de 75 años por CI en España en el periodo 1998-2018, diferenciando por provincias.
Métodos: Estudio observacional de tendencias temporales de la mortalidad prematura por CI en España, provincial y por sexo en 1998-2018. La población abarca a los ciudadanos residentes con edades entre 0 y 74 años. Las fuentes de datos son el padrón continuo poblacional y el registro de defunciones del Instituto Nacional de Estadística. Se calcularon tasas de mortalidad ajustadas por edad y sus porcentajes de cambio medio anual estimados por modelos de Poisson.
Resultados: Se observó en el periodo de estudio un descenso generalizado de las tasas de mortalidad por CI, tanto en España como por provincias, del 53% en varones y el 61% en mujeres, y con un porcentaje de cambio medio anual de –3,92 y –5,07 respectivamente. El primer año (1998) se observó una distribución de la mortalidad desigual entre provincias, mayor en el sur peninsular.
Conclusiones: Se constató un importante descenso de la mortalidad prematura por CI en España durante el periodo de estudio y en ambos sexos, hasta la mitad de los casos iniciales. Este descenso fue estadísticamente significativo en prácticamente todas las provincias. Las diferencias interprovinciales de mortalidad y sus variaciones se están amortiguando en los años más recientes.

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Abbreviations

AAMR: age-adjusted mortality rate
AAPC: average annual percent change
AC: autonomous community
CVRF: cardiovascular risk factor
IHD: ischemic heart disease
PM: premature mortality

INTRODUCTION

Cardiovascular disease is the leading cause of death[1] and hospitalization[2] in Spain and in the European Union.[3] Ischemic heart disease (IHD) is itself the most common cause of cardiovascular mortality[4] and the primary cause of death worldwide.[5] In Spain, death due to IHD reached 7.8% of all deaths in 2016, with significant differences by sex. The percentage is higher in men, in whom it has been the leading cause of death since 1987; meanwhile, it is the second most common cause of death in women after stroke.[4,6]

In developed countries, death due to IHD has fallen since 1975, although the reduction has slowed since 1990.[7,8] The decline has been attributed both to improved treatment of acute coronary syndrome and to preventive measures.[9] The incidence of IHD significantly differs by age and sex,[10] similar to IHD mortality,[11] which rapidly increases with age, and the rates in women are approximately the same as those of men who are 10 years younger.

Prevalence also increases with age and differs by sex. Data from the United States show a predominance of men in terms of both overall IHD and myocardial infarction in particular in all age groups.[12] In Spain, there are no data on the true prevalence of IHD but population surveys[13] include myocardial infarction and permit indirect estimates, which indicate lower rates vs America at all ages and a reduction from 2006 to 2012.[9]

In addition to premature mortality (PM) due to IHD, people who survive the acute phase become chronic patients, with slow progression and quality of life limitations that affect their caregivers. The economic effects are considerable for families and society and undermine the sustainability of the health care system. Accordingly, cardiovascular disease is estimated to cause more than 50% of health expenditure costs and almost 25% of productivity losses in Europe.[14] Thus, our actions must include deep and ongoing studies.

Previous studies of death due to IHD in Spain[2,15–17] differ in the periods covered and other parameters. In contrast to the present study, none included data until 2018 differentiated by sex and region. PM due to IHD has also not been studied by autonomous community (AC), unlike that due to heart failure.[18] Accordingly, the objective of this study was to analyze the trends in PM due to IHD in Spain from 1998 to 2018 by province.

METHODS

This observational study examined trends in PM due to IHD in Spain by province from 1998 to 2018. PM was defined as any death due to IHD in individuals younger than 75 years old (key indicators for the Spanish National Health System[19]). PM due to IHD was analyzed in residents of Spain aged between 0 and 74 years and by province. A national analysis was also performed of groups aged 0 to 34, 35 to 64, and 65 to 74 years. The basic cause of death was defined by ICD-9 codes 410 to 414 (1998) and ICD-10 codes I20 to I25 (1999-2018) of the International Classification of Diseases (ICD) Ninth and Tenth revisions. We excluded patients with no record of their province of residence.

The population data source used was the continuous population register of the Spanish National Institute of Statistics (INE).[20] We additionally used the cause of death recorded in the mortality registry, also available at the electronic portal of this institute.

The study variables were populations by age, sex, year, and province of residence, as well as province of residence, age in years, sex, and year of death.

Statistical analysis

Age-adjusted mortality rates (AAMRs)/100 000 population were calculated via the direct method, as well as their corresponding 95% confidence intervals (95%CIs), by age and sex and both nationally and for each province. For standardization, we used the European standard population for 2013 published by Eurostat[21]; the population each year was divided into 5-year age groups by province and sex, with the corresponding 95%CI, and truncated rates were calculated in each age group. Although the objective of this study was centered on PM, the national AAMR was also calculated in individuals older than 74 years by age and sex to fully analyze the mortality trends. To assess the change in mortality over the study period, Poisson regression models were adjusted to the logarithm of the number of deaths, using the logarithm of the population as offset and adjusting by groups aged < 50, 50 to 64, and 65 to 74 years. The average annual percent change (AAPC) in mortality was estimated using the expression $(\exp(\beta) - 1)\cdot 100\%$, where β corresponds to the variable year of death. The 95%CI was calculated for the AAPC and the values were estimated by province and sex. All analyses were performed with the statistical program R 4.0.2.[22]

RESULTS

In total, 232 617 premature deaths due to IHD were analyzed during the study period; 181 424 (78.0%) occurred in men and 51 193 (22.0%) in women.

In 1998, PM due to IHD occurred in 14 876 people in Spain, 11 234 men (75.5%) and 3642 women (24.5%). In 2018, PM due to IHD occurred in 8780, 7036 men (80.1%) and 1744 women (19.8%). PM due to IHD in individuals younger than 75 years represented 30.9% of total mortality due to IHD. Table 1 of the supplementary data and table 2 of the supplementary data show the number of deaths and the AAMRs and 95%CIs of death due to IHD in Spain by province during the entire study period and in both sexes.

Table 1 and table 2 show the national AAMR of all years for men and women, respectively, with those younger than 74 years differentiated by groups aged 0 to 34, 45 to 64, and 65 to 74 years, in addition to those aged $>$ 74 years. There was a fall in the mortality rates of all age groups, although it was more pronounced in those older than 35 years, in both men and women. Although the magnitude of the mortality due to IHD was much higher in people older than 74 years, a similar decreasing pattern was detected in both age groups during the study period.

Table 3 shows the national AAMRs and those of each province in 1998 and 2018 for men, as well as the AAPC and 95%CI for the entire period. The national AAMR for men was 75.5 deaths/100 000 population in 1998 and 35.3/100 000 in 2018. Regarding the values of the AAPC index in men during the study period, the national average changed by −3.92% per year (Table 3). The geographical distribution

Table 1
Death due to ischemic heart disease in men in Spain by age group from 1998 to 2018

Year	0-74 y			0-34 y			35-64 y			65-74 y			> 74 y		
	n	AAMR	95%CI	n	AAMR	95%CI	n	AAMR	95%CI	n	AAMR	95%CI	n	AAMR	95%CI
1998	11 234	75.5	(74.1-76.9)	114	1.1	(0.9-1.3)	4729	70.9	(68.9-72.9)	6391	376.5	(367.2-385.7)	11 118	1192.6	(1170.0-1215.2)
1999	11 336	74.6	(73.2-75.9)	104	1.0	(0.8-1.2)	4627	68.8	(66.8-70.8)	6605	377.1	(368.0-386.2)	11 340	1161.8	(1140.0-1183.7)
2000	10 978	71.8	(70.4-73.1)	108	1.0	(0.8-1.2)	4553	67.6	(65.6-69.6)	6317	357.5	(348.6-366.3)	11 095	1097.4	(1076.5-1118.2)
2001	10 340	66.5	(65.2-67.8)	95	0.9	(0.7-1.0)	4293	62.7	(60.8-64.6)	5952	331.0	(322.6-339.5)	11 384	1076.3	(1056.1-1096.5)
2002	10 121	64.2	(62.9-65.4)	105	0.9	(0.8-1.1)	4243	61.0	(59.2-62.9)	5773	317.1	(308.9-325.3)	11 698	1073.7	(1053.8-1093.7)
2003	10 159	63.3	(62.1-64.6)	112	1.0	(0.8-1.1)	4305	60.4	(58.6-62.3)	5742	312.2	(304.1-320.3)	12 344	1104.2	(1084.2-1124.3)
2004	9355	57.7	(56.5-58.8)	99	0.8	(0.7-1.0)	4146	56.0	(54.2-57.7)	5110	280.7	(273.0-288.4)	12 096	1048.0	(1028.7-1067.3)
2005	9443	57.7	(56.6-58.9)	88	0.7	(0.6-0.9)	4147	53.7	(52.1-55.4)	5208	290.3	(282.4-298.2)	12 342	1031.4	(1012.6-1050.2)
2006	8976	53.9	(52.8-55.0)	71	0.6	(0.4-0.7)	4224	53.6	(51.9-55.2)	4681	258.3	(250.9-265.7)	11 868	952.8	(935.1-970.5)
2007	8758	52.2	(51.1-53.3)	80	0.7	(0.5-0.8)	4134	51.2	(49.6-52.7)	4544	252.4	(245.1-259.8)	12 164	949.2	(931.8-966.6)
2008	8173	48.0	(47.0-49.1)	79	0.6	(0.5-0.8)	4035	48.3	(46.8-49.8)	4059	227.2	(220.2-234.2)	11 837	886.7	(870.3-903.1)
2009	7891	45.9	(44.9-47.0)	100	0.8	(0.7-1.0)	3910	45.9	(44.4-47.3)	3881	218.0	(211.2-224.9)	12 166	871.8	(855.9-887.6)
2010	7578	43.8	(42.8-44.8)	83	0.7	(0.6-0.9)	3784	43.5	(42.1-44.9)	3711	209.4	(202.7-216.2)	12 346	853.5	(838.2-868.8)
2011	7183	40.9	(40.0-41.9)	76	0.6	(0.5-0.8)	3559	40.4	(39.1-41.8)	3548	196.3	(189.8-202.8)	12 416	825.2	(810.5-839.9)
2012	7129	40.2	(39.3-41.2)	57	0.5	(0.4-0.6)	3606	40.2	(38.9-41.6)	3466	191.4	(185.0-197.8)	12 504	803.3	(789.0-817.5)
2013	7179	39.8	(38.9-40.7)	57	0.5	(0.4-0.7)	3700	40.8	(39.5-42.1)	3422	185.7	(179.4-191.9)	11 892	743.2	(729.7-756.8)
2014	7176	39.2	(38.3-40.1)	47	0.5	(0.3-0.6)	3665	40.2	(38.9-41.5)	3464	182.7	(176.6-188.9)	11 516	711.5	(698.4-724.6)
2015	7163	38.0	(37.2-38.9)	43	0.5	(0.3-0.6)	3597	39.2	(37.9-40.4)	3523	177.0	(171.2-182.9)	12 029	730.5	(717.3-743.7)
2016	7132	37.4	(36.6-38.3)	39	0.4	(0.3-0.6)	3622	38.6	(37.4-39.9)	3471	173.9	(168.1-179.7)	11 493	678.7	(666.2-691.2)
2017	7084	36.4	(35.6-37.3)	33	0.4	(0.2-0.5)	3544	37.1	(35.9-38.3)	3507	171.3	(165.6-177.0)	11 641	672.6	(660.3-684.9)
2018	7036	35.3	(34.5-36.2)	43	0.5	(0.3-0.6)	3607	37.2	(36.0-38.4)	3386	160.9	(155.4-166.3)	10 983	621.8	(610.1-633.5)

95%CI, 95% confidence interval; AAMRs, age-adjusted mortality rates/100 000 population (direct method, European standard population for 2013).

Table 2
Death due to ischemic heart disease in women in Spain by age group from 1998 to 2018

Year	0-74 y			0-34 y			35-64 y			65-74 y			> 74 y		
	n	AAMR	95%CI	n	AAMR	95%CI	n	AAMR	95%CI	n	AAMR	95%CI	n	AAMR	95%CI
1998	3642	21.2	(20.5-21.8)	28	0.3	(0.2-0.4)	853	12.2	(11.4-13.0)	2761	135.3	(130.2-140.3)	13 448	789.7	(776.4-803.1)
1999	3609	20.5	(19.8-21.2)	32	0.3	(0.2-0.4)	878	12.4	(11.6-13.3)	2699	128.5	(123.7-133.4)	13 711	769.7	(756.8-782.6)
2000	3416	19.3	(18.7-20.0)	22	0.2	(0.1-0.3)	783	11.2	(10.4-12.0)	2611	123.5	(118.8-128.2)	13 199	714.2	(702.1-726.4)
2001	3274	18.3	(17.6-18.9)	25	0.2	(0.1-0.3)	785	11.1	(10.3-11.8)	2464	114.7	(110.2-119.2)	13 189	683.2	(671.5-694.9)
2002	3045	16.9	(16.3-17.5)	18	0.2	(0.1-0.2)	789	11.1	(10.3-11.8)	2238	103.1	(98.8-107.4)	13 929	707.0	(695.3-718.8)
2003	3074	16.9	(16.3-17.5)	10	0.1	(0.0-0.2)	814	11.2	(10.5-12.0)	2250	102.7	(98.4-106.9)	14 209	702.7	(691.2-714.3)
2004	2883	15.8	(15.2-16.3)	13	0.1	(0.1-0.2)	765	10.2	(9.5-10.9)	2105	96.8	(92.6-100.9)	13 931	670.9	(659.8-682.1)
2005	2746	14.9	(14.4-15.5)	22	0.2	(0.1-0.3)	787	10.0	(9.3-10.7)	1937	90.1	(86.1-94.1)	14 252	664.2	(653.3-675.1)
2006	2485	13.4	(12.9-13.9)	13	0.1	(0.1-0.2)	745	9.2	(8.5-9.8)	1727	80.3	(76.5-84.1)	13 309	599.2	(589.0-609.4)
2007	2461	13.3	(12.7-13.8)	28	0.3	(0.2-0.4)	741	8.9	(8.3-9.6)	1692	79.5	(75.7-83.3)	13 409	586.9	(576.9-596.8)
2008	2280	12.2	(11.7-12.8)	18	0.2	(0.1-0.2)	694	8.1	(7.5-8.7)	1568	74.3	(70.6-78.0)	13 164	553.7	(544.3-563.2)
2009	2014	10.8	(10.3-11.3)	13	0.1	(0.1-0.2)	665	7.6	(7.0-8.1)	1336	64.0	(60.6-67.5)	13 205	533.4	(524.2-542.5)
2010	1984	10.7	(10.2-11.2)	25	0.2	(0.1-0.3)	671	7.5	(7.0-8.1)	1288	62.8	(59.4-66.2)	12 967	505.2	(496.5-513.9)
2011	1880	10.0	(9.6-10.5)	16	0.1	(0.1-0.2)	651	7.2	(6.7-7.8)	1213	58.3	(55.0-61.6)	12 933	485.2	(476.8-493.6)
2012	1861	9.9	(9.4-10.3)	9	0.1	(0.0-0.2)	718	7.8	(7.2-8.4)	1134	55.0	(51.8-58.2)	12 828	464.3	(456.3-472.4)
2013	1768	9.3	(8.8-9.7)	13	0.1	(0.1-0.2)	688	7.4	(6.8-7.9)	1067	51.3	(48.2-54.4)	12 156	429.9	(422.2-437.6)
2014	1714	8.8	(8.4-9.2)	9	0.1	(0.0-0.2)	662	7.1	(6.5-7.6)	1043	48.5	(45.6-51.5)	11 639	401.8	(394.4-409.1)
2015	1801	8.9	(8.5-9.4)	8	0.1	(0.0-0.1)	668	7.1	(6.5-7.6)	1125	49.9	(47.0-52.8)	12 306	415.6	(408.1-423.0)
2016	1710	8.4	(8.0-8.8)	12	0.1	(0.1-0.2)	671	7.0	(6.5-7.5)	1027	45.3	(42.6-48.1)	11 173	367.6	(360.7-374.5)
2017	1802	8.6	(8.2-9.0)	5	0.1	(0.0-0.1)	704	7.2	(6.6-7.7)	1093	46.9	(44.1-49.6)	11 275	362.1	(355.3-368.9)
2018	1744	8.2	(7.8-8.5)	3	0.0	(0.0-0.1)	674	6.7	(6.2-7.2)	1067	44.5	(41.9-47.2)	10 882	345.1	(338.5-351.8)

95%CI, 95% confidence interval; AAMRs, age-adjusted mortality rates/100 000 population (direct method, European standard population for 2013).

Table 3
Premature mortality due to ischemic heart disease in men in Spanish provinces and the average annual percent change between 1998 and 2018

Area	1998			2018			AAPC, %	95%CI
	n	AAMR	95%CI	n	AAMR	95%CI		
National	11 234	75.5	(74.1-76.9)	7036	35.3	(34.5-36.2)	−3.92	(−4.15; −3.70)
Álava	63	59.0	(44.2-73.8)	32	21.2	(13.9-28.6)	−4.34	(−5.33; −3.33)
Albacete	82	58.1	(45.4-70.8)	53	33.1	(24.0-42.1)	−3.32	(−4.19; −2.44)
Alicante	489	94.5	(86.1-102.9)	328	39.6	(35.3-43.9)	−4.15	(−4.60; −3.69)
Almería	152	91.6	(76.9-106.2)	97	36.4	(29.0-43.7)	−4.17	(−4.98; −3.35)
Principality of Asturias	415	88.4	(79.9-97.0)	248	46.9	(41.1-52.8)	−2.92	(−3.37; −2.47)
Ávila	52	62.7	(45.4-80.0)	18	22.0	(11.8-32.2)	−3.93	(−5.05; −2.80)
Badajoz	193	77.2	(66.2-88.2)	99	34.0	(27.3-40.8)	−3.91	(−4.60; −3.21)
Balearic Islands	218	79.7	(69.0-90.3)	151	34.0	(28.5-39.5)	−3.89	(−4.59; −3.18)
Barcelona	1220	69.3	(65.4-73.2)	677	29.5	(27.2-31.7)	−4.46	(−4.83; −4.09)
Burgos	78	52.2	(40.5-63.9)	63	35.1	(26.4-43.7)	−2.31	(−3.16; −1.45)
Cáceres	139	78.7	(65.5-91.9)	72	38.5	(29.5-47.4)	−3.72	(−4.41; −3.03)
Cádiz	326	100.8	(89.7-111.9)	220	43.6	(37.8-49.4)	−4.17	(−4.58; −3.75)
Cantabria	128	60.8	(50.2-71.4)	91	33.4	(26.5-40.4)	−3.53	(−4.39; −2.67)
Castellón	168	91.7	(77.8-105.7)	83	33.3	(26.1-40.5)	−4.15	(−4.84; −3.45)
Autonomous City of Ceuta	21	108.4	(61.5-155.2)	6	20.1	(3.3-36.9)	−5.24	(−6.98; −3.47)
Ciudad Real	115	57.8	(47.1-68.5)	61	29.1	(21.8-36.5)	−2.96	(−3.67; −2.24)
Córdoba	227	83.0	(72.1-93.8)	116	35.6	(29.1-42.2)	−4.69	(−5.33; −4.05)
A Coruña	325	74.7	(66.6-82.9)	198	36.9	(31.8-42.1)	−3.76	(−4.28; −3.23)
Cuenca	54	52.1	(37.9-66.3)	22	25.0	(14.5-35.6)	−3.26	(−4.42; −2.08)
Girona	128	59.3	(49.0-69.6)	99	30.7	(24.6-36.7)	−3.53	(−4.34; −2.71)
Granada	282	97.8	(86.3-109.4)	176	46.5	(39.6-53.5)	−4.08	(−4.56; −3.60)
Guadalajara	37	55.5	(37.1-73.8)	25	23.8	(14.3-33.4)	−3.72	(−4.88; −2.55)
Guipúzcoa	174	65.8	(55.9-75.6)	86	25.1	(19.8-30.4)	−4.40	(−5.02; −3.77)
Huelva	138	89.5	(74.5-104.5)	107	51.5	(41.7-61.3)	−4.27	(−5.04; −3.49)
Huesca	56	55.5	(40.7-70.2)	40	38.2	(26.3-50.1)	−3.00	(−4.34; −1.63)
Jaén	159	66.4	(55.9-76.8)	95	36.3	(28.9-43.7)	−2.54	(−3.16; −1.92)
Las Palmas de Gran Canaria	331	134.2	(119.3-149.1)	282	61.0	(53.7-68.3)	−4.80	(−5.48; −4.11)
León	138	58.9	(48.9-68.9)	88	37.8	(29.9-45.8)	−2.51	(−3.32; −1.69)
Lleida	87	54.7	(43.0-66.3)	49	26.8	(19.2-34.4)	−5.72	(−6.60; −4.82)
Lugo	145	83.5	(69.6-97.3)	72	42.7	(32.8-52.5)	−3.23	(−3.92; −2.55)
Community of Madrid	1073	62.2	(58.5-66.0)	732	28.6	(26.5-30.7)	−4.33	(−4.70; −3.95)
Málaga	434	104.8	(94.9-114.8)	313	45.7	(40.6-50.8)	−4.00	(−4.37; −3.63)
Autonomous City of Melilla	13	82.7	(37.5-127.9)	13	46.0	(19.5-72.5)	−4.21	(−6.19; −2.18)
Region of Murcia	296	78.1	(69.1-87.0)	192	33.9	(29.0-38.7)	−3.66	(−4.22; −3.11)
Chartered Community of Navarre	144	68.2	(57.0-79.4)	70	24.0	(18.3-29.6)	−4.77	(−5.43; −4.10)
Ourense	119	71.0	(58.1-83.9)	47	28.5	(20.4-36.7)	−3.88	(−4.75; −3.00)
Palencia	45	59.7	(42.0-77.4)	37	43.6	(29.5-57.8)	−2.38	(−3.44; −1.31)
Pontevedra	211	65.1	(56.3-74.0)	123	28.6	(23.5-33.7)	−3.90	(−4.53; −3.25)
La Rioja	70	63.4	(48.5-78.3)	48	33.9	(24.3-43.5)	−3.18	(−4.11; −2.24)
Santa Cruz de Tenerife	262	106.0	(93.0-119.0)	217	50.3	(43.6-57.1)	−3.76	(−4.37; −3.15)
Salamanca	106	71.2	(57.5-84.9)	43	26.1	(18.3-33.9)	−4.92	(−5.75; −4.09)
Segovia	29	41.3	(26.2-56.3)	24	32.2	(19.2-45.2)	−2.25	(−3.73; −0.76)
Seville	552	103.7	(95.0-112.4)	366	48.6	(43.5-53.6)	−4.25	(−4.69; −3.81)
Soria	20	42.6	(23.8-61.5)	15	35.5	(17.4-53.6)	−3.54	(−5.17; −1.89)
Tarragona	155	67.5	(56.9-78.2)	123	35.6	(29.3-41.9)	−2.97	(−3.60; −2.35)
Teruel	45	60.9	(42.5-79.3)	19	29.6	(16.2-43.0)	−3.37	(−4.68; −2.04)
Toledo	143	66.8	(55.8-77.9)	79	28.0	(21.7-34.2)	−4.98	(−5.65; −4.30)
Valencia	663	83.6	(77.2-89.9)	381	35.7	(32.1-39.3)	−4.26	(−4.66; −3.85)
Valladolid	114	61.3	(50.0-72.6)	76	30.1	(23.3-36.9)	−2.91	(−3.75; −2.05)
Vizcaya	306	66.3	(58.8-73.8)	185	33.5	(28.7-38.4)	−3.13	(−3.68; −2.58)
Zamora	48	48.2	(34.2-62.1)	30	33.0	(21.1-44.9)	−3.15	(−4.20; −2.09)
Zaragoza	246	69.7	(60.9-78.4)	149	35.1	(29.4-40.7)	−3.69	(−4.26; −3.11)

95%CI, 95% confidence interval; AAMRs, age-adjusted mortality rates/100 000 population (direct method, European standard population for 2013); AAPC, average annual percent change estimated by Poisson models.

of the provincial variations in the mortality rates of men in 1998 are presented in figure 1. Higher-than-average rates were found in Andalusia, the Valencian Community, and the nonmainland autonomous communities, followed by Extremadura and Region of Murcia. In the north half of the country, higher-than-average rates were only seen in Principality of Asturias and the province of Lugo. There was a significant decrease in the AAPC of men during the study period in all provinces (figure 2).

In women, the national AAMRs were 21.2 deaths/100 000 population in 1998 and 8.2/100 000 in 2018 (table 4). The AAPC index values in women during the entire period were always negative and significant in all Spanish provinces, with a national average of −5.07%. The lower part of figure 1 illustrates the geographical distribution of the provincial variations in the mortality rates of women in 1998. The most unfavorable rates were found in the autonomous communities in the south and east, as well as in the Autonomous City of Melilla. In the north, only the Principality of Asturias and the province of A Coruña slightly exceeded the average. In the center, in contrast to the situation for men, higher-than-average rates were found in the provinces of Soria and Cuenca. As shown in the lower part of figure 2, the AAPC of women significantly decreased in all provinces.

Figure 3 illustrates the national mortality trends from 1998 to 2018 in individuals younger and older than 74 years. For men and women younger than 74 years, the fall was uniform, with very small fluctuations. Although the magnitude was greater, the same pattern of reduced mortality was seen in those older than 74 years. The initial PM figures fell to practically half at the end of the study period. In addition, throughout the entire period, PM due to IHD in men was slightly more than 3 times that in women.

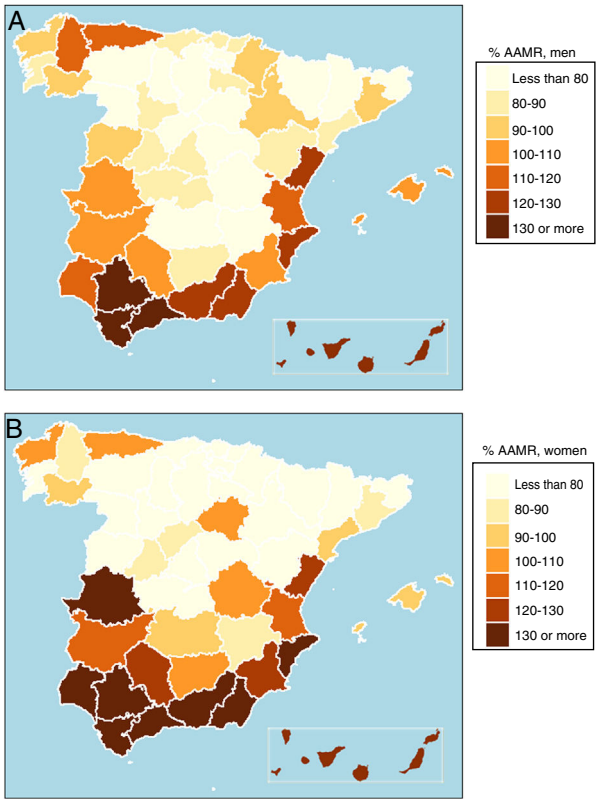

Figure 1. Territorial differences in death due to ischemic heart disease in 1998. A: mortality rate in men (percentage) vs the national rate (75.5 deaths/100 000 population). B: mortality rate in women (percentage) vs the national rate (21.2 deaths/100 000 population). AAMR, age-adjusted mortality rate.

DISCUSSION

This study reveals a widespread decrease in the mean PM due to IHD from 1998 to 2018 at both the national and provincial levels that, on average, was more pronounced in women than in men (53% vs 61%). The geographical variations in the PM rates were heterogeneously distributed. The 3 regions exhibiting the greatest decrease in men were Lleida, Ceuta, and Toledo, whereas Palencia, Burgos, and Segovia showed the lowest decrease. In women, the 3 regions with the greatest decreases were Córdoba, Region of Murcia, and Barcelona; the lowest decreases were seen in Ceuta, León, and Palencia.

Our results are in agreement with those of the Spanish Health Information Institute (IIS),[15] which covered the period from 1990 to 2006 and concluded that the ACs with the worst AAMRs are in the south (Andalusia, the Canary Islands, and the Autonomous Cities of Ceuta and Melilla) and the Valencian Community. The data are also in line with those reported by Boix et al.,[17] who analyzed the period from 1988 to 1997 and the population aged between 35 and 64 years. The present study confirms that there was a reduction in mortality rates at the national level from 1998 to 2018, which is sustained[17] and significant in all provinces and in both sexes. These results thus answer some of the questions raised by Boix et al.[17] In addition, their results show that the north-south divide in Spain is maintained in the study period and they mention possible factors that could contribute to this heterogeneity,[17] such as the geographical differences and the trends in the prevalence of cardiovascular risk factors (CVRFs), socioeconomic level, and health care quality and access. The results of the present study are also in line with the fall in acute myocardial infarction mortality observed by Dégano et al.,[5] who estimated AAPC decreases of −4.4 and −7.3 in men and women in the province

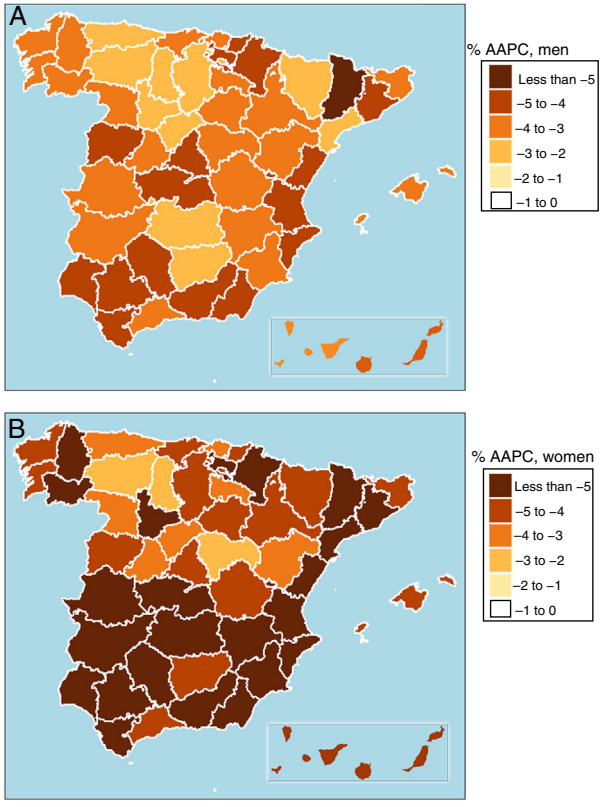

Figure 2. Death due to ischemic heart disease: average annual percent change (AAPC) by province from 1998 to 2018. A: men. B: women.

Table 4
Premature mortality due to ischemic heart disease in women in Spanish provinces and the average annual percent change between 1998 and 2018

Area	1998			2018			AAPC, %	95%CI
	n	AAMR	95%CI	n	AAMR	95%CI		
National	3642	21.2	(20.5-21.8)	1744	8.2	(7.8-8.5)	−5.07	(−5.48; −4.66)
Álava	13	12	(5.5-18.5)	8	5	(1.5-8.5)	−5.46	(−7.73; −3.13)
Albacete	29	18.3	(11.6-25.1)	11	6.9	(2.8-11.0)	−5.75	(−7.44; −4.03)
Alicante	180	31	(26.5-35.5)	98	11.1	(8.9-13.3)	−5.22	(−5.83; −4.61)
Almería	52	28.4	(20.7-36.2)	27	10.2	(6.3-14.0)	−5.53	(−6.67; −4.37)
Principality of Asturias	126	22.1	(18.2-26.0)	70	11.8	(9.0-14.5)	−3.31	(−4.28; −2.33)
Ávila	17	18.6	(9.5-27.8)	2	2.7	(0.0-6.4)	−3.96	(−6.16; −1.70)
Badajoz	71	23.8	(18.2-29.3)	29	9.7	(6.2-13.3)	−5.92	(−6.91; −4.92)
Balearic Islands	64	20.6	(15.6-25.7)	31	6.7	(4.3-9.1)	−4.71	(−5.74; −3.68)
Barcelona	384	18.4	(16.5-20.2)	113	4.4	(3.6-5.2)	−6.53	(−7.20; −5.85)
Burgos	13	7.3	(3.3-11.4)	6	3.4	(0.7-6.2)	−4.02	(−6.34; −1.64)
Cáceres	57	28.8	(21.2-36.4)	15	7.9	(3.9-11.9)	−6.44	(−7.78; −5.08)
Cádiz	128	34.9	(28.8-41.0)	68	12.8	(9.8-15.9)	−5.06	(−5.73; −4.39)
Cantabria	35	14.5	(9.7-19.4)	15	5.2	(2.6-7.8)	−4.45	(−5.90; −2.98)
Castellón	56	27	(19.9-34.0)	16	6.3	(3.2-9.3)	−6.32	(−7.50; −5.12)
Autonomous City of Ceuta	11	50.1	(20.4-79.8)	6	22.8	(4.3-41.4)	−2.84	(−5.39; −0.21)
Ciudad Real	46	20.7	(14.6-26.7)	12	5.5	(2.4-8.6)	−6.06	(−7.29; −4.82)
Córdoba	89	27.4	(21.7-33.2)	22	6.5	(3.8-9.3)	−7.37	(−8.38; −6.35)
A Coruña	115	22.2	(18.1-26.3)	46	7.6	(5.4-9.8)	−4.52	(−5.48; −3.55)
Cuenca	24	21.5	(12.7-30.3)	4	4.8	(0.1-9.5)	−4.99	(−7.21; −2.72)
Girona	31	13.4	(8.7-18.2)	24	7.7	(4.6-10.7)	−4.59	(−6.03; −3.13)
Granada	107	31.8	(25.7-37.8)	43	10.9	(7.6-14.2)	−5.23	(−6.06; −4.40)
Guadalajara	10	12.6	(4.8-20.4)	7	8	(2.0-14.0)	−2.91	(−5.33; −0.43)
Guipúzcoa	40	13.4	(9.2-17.5)	24	6.5	(3.9-9.1)	−4.88	(−6.30; −3.44)
Huelva	53	30	(21.9-38.1)	20	9	(5.0-12.9)	−5.38	(−6.51; −4.24)
Huesca	13	12.3	(5.5-19.0)	4	4	(0.1-7.9)	−4.12	(−6.23; −1.96)
Jaén	59	21.5	(15.9-27.0)	25	9	(5.5-12.6)	−4.35	(−5.67; −3.00)
Las Palmas de Gran Canaria	116	44.8	(36.5-53.0)	88	19.4	(15.3-23.4)	−5.59	(−6.44; −4.74)
León	31	11.8	(7.6-16.1)	18	7.5	(4.0-10.9)	−2.68	(−4.43; −0.90)
Lleida	30	16.6	(10.6-22.6)	9	4.8	(1.7-8.0)	−5.79	(−7.47; −4.08)
Lugo	40	18.6	(12.7-24.5)	11	6.2	(2.5-9.9)	−5.21	(−6.67; −3.74)
Community of Madrid	280	13.6	(12.0-15.2)	199	6.7	(5.7-7.6)	−4.33	(−5.10; −3.55)
Málaga	140	29.8	(24.9-34.8)	88	11.9	(9.4-14.4)	−4.98	(−5.63; −4.32)
Autonomous City of Melilla	4	20.8	(0.4-41.1)	3	13.5	(0.0-29.0)	−4.16	(−7.35; −0.87)
Region of Murcia	115	26.5	(21.7-31.4)	43	7.6	(5.3-9.8)	−6.76	(−7.71; −5.80)
Chartered Community of Navarre	37	15.9	(10.8-21.0)	15	5.3	(2.6-7.9)	−5.22	(−6.84; −3.57)
Ourense	45	21.2	(14.9-27.4)	11	6.4	(2.6-10.3)	−5.41	(−6.89; −3.90)
Palencia	15	17	(8.0-25.9)	5	6	(0.7-11.4)	−2.63	(−4.79; −0.43)
Pontevedra	60	15.5	(11.6-19.5)	40	8.2	(5.7-10.8)	−4.75	(−5.84; −3.64)
La Rioja	11	8.5	(3.5-13.6)	11	7.5	(3.0-11.9)	−3.58	(−5.52; −1.60)
Salamanca	23	12	(7.1-16.9)	6	3.4	(0.7-6.1)	−4.56	(−6.48; −2.59)
Santa Cruz de Tenerife	96	34.6	(27.6-41.5)	62	14	(10.5-17.4)	−5.23	(−6.24; −4.20)
Segovia	14	18.6	(8.7-28.5)	8	12	(3.7-20.3)	−3.02	(−5.63; −0.33)
Seville	223	35.7	(31.0-40.4)	109	13	(10.6-15.5)	−5.38	(−6.04; −4.71)
Soria	12	23.1	(9.8-36.5)	3	7.4	(0.0-15.7)	−4.97	(−8.82; −0.95)
Tarragona	52	20.5	(14.9-26.0)	31	8.8	(5.7-11.9)	−5.02	(−6.17; −3.85)
Teruel	12	14.9	(6.4-23.4)	7	11.6	(3.0-20.2)	−3.97	(−6.49; −1.39)
Toledo	30	12.5	(8.0-17.0)	20	7.3	(4.1-10.5)	−5.28	(−6.86; −3.67)
Valencia	232	24.8	(21.6-27.9)	95	8.1	(6.4-9.7)	−5.81	(−6.36; −5.26)
Valladolid	33	15.9	(10.5-21.4)	19	7	(3.9-10.2)	−5.24	(−7.00; −3.43)
Vizcaya	86	16.6	(13.1-20.1)	49	8.1	(5.8-10.4)	−3.84	(−4.76; −2.92)
Zamora	17	12.7	(6.7-18.8)	9	9.8	(3.4-16.3)	−3.44	(−5.50; −1.35)
Zaragoza	65	15.8	(12.0-19.7)	39	8.5	(5.8-11.1)	−4.21	(−5.22; −3.19)

95%CI, 95% confidence interval; AAMRs, age-adjusted mortality rates/100 000 population (direct method, European standard population for 2013); AAPC, average annual percent change estimated by Poisson models.

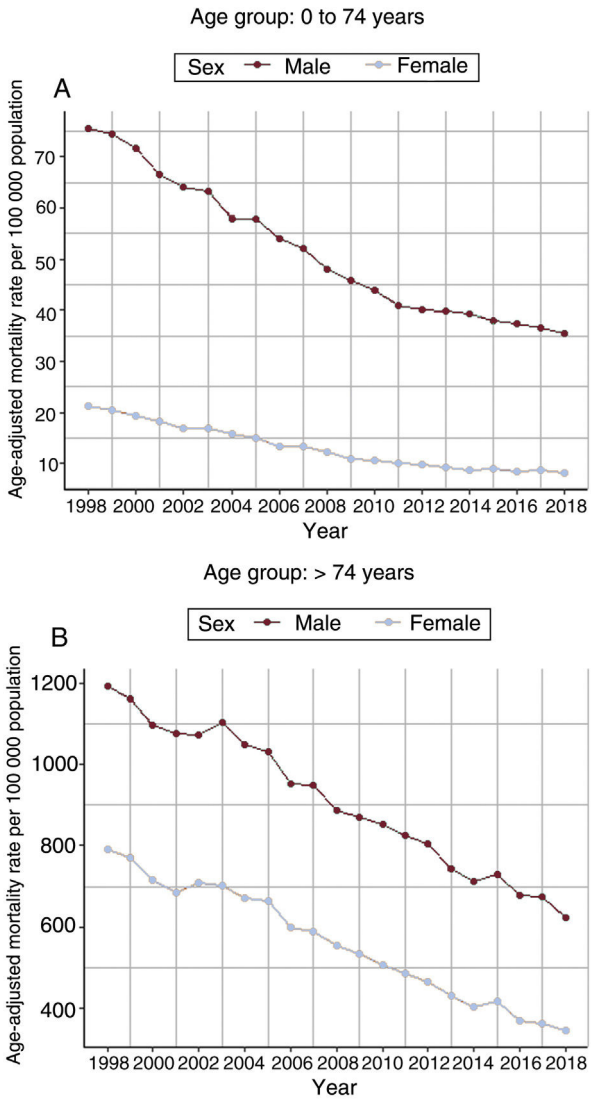

Figure 3. Annual trends in mortality due to ischemic heart disease adjusted by age from 1998 to 2018 in men and women in Spain and by age 0 to 74 years (A) and > 74 years (B).

of Girona between 1985 and 2010, although the rates were calculated using a different methodology.

Differences among ACs have been found and analyzed in other studies, such as that by Banegas et al.[2] in 2006, which also indicated that the geographical variability was similar to that seen in other cardiovascular diseases. Gómez-Martínez et al.,[18] from 1999 to 2013, found a generalized mean decrease, both national and by AC, in PM due to heart failure in Spain that was also more pronounced in women than in men.

Progress has been made in the understanding of CVRFs in Spain in recent years.[2,15–17,23,24] Modifiable CVRFs can be addressed in primary and secondary prevention. As shown in table 1, the pattern of the decline appears to be similar in age groups lower and higher than 74 years, indicating that there is no generational delay in the onset of fatal and nonfatal IHD events. The ERICE study,[25] published in 2008, found that the major burden of CVRFs was present in the southeast and Mediterranean regions of Spain, with the lowest burden in the north and center. In 2010, the DARIOS study[26] determined that the Canary Islands, Andalusia, and Extremadura had higher mortality due to IHD and higher prevalence of obesity, diabetes mellitus, hypertension, and dyslipidemia in both sexes. Recently, Orozco Beltrán et al.[23] also found a heterogeneous geographical distribution, with excess mortality due to diabetes in southern and southeastern provinces. However, they also observed that the previous north-south divide ameliorated in 2008 and even disappeared in 2013, concluding that "these findings strengthen the hypothesis that the advances in primary, secondary, and tertiary prevention and the new drugs approved in these years have smoothened the mortality rates between patients with and without diabetes mellitus and that a higher prevalence would not necessarily equal higher mortality".

Although the association between CVRFs and PM due to IHD does not allow us to make definitive conclusions and more studies are required, it seems reasonable to suppose that the worse behavior in the abovementioned regions is primarily due to their worse situation in terms of risk factors because there is no evidence that it can be attributed to other causes in this age group, such as differences in treatment or demographics.[27]

It is reasonable to attribute the observed behavior both to improvements in treatments and early diagnoses and to changes in the prevalence of risk factors, as has been postulated previously. Notably, the Infarction Code Program had not yet been implemented in most ACs in the period of this study, although catheterization units were operating in some hospitals. The implementation of the Infarction Code Program was recommended in 2009 in the Ischemic Heart Disease Strategy document of the Spanish National Health System[28] and was introduced in the different ACs at different speeds.

Regardless, we consider it vital to continue investigating the regional differences in the trends in mortality due to IHD and in their causes to design and trial approaches aimed at reducing the incidence and lethality of this disease. All preventive measures to improve the control of CVRFs will culminate in additional improvements in the rates of mortality due to cardiovascular diseases and, consequently, of PM due to IHD.

Limitations

A possible limitation that would affect all studies of mortality would be related to the variability among regions in the coding of the basic cause of death, despite the application of standardized coding methods. The INE periodically reports the methodology and validity of the selection and grouping of the main causes of death. Spanish mortality data are treated and validated in the provincial delegations, in the different ACs, and in the central headquarters of the INE. This process can be consulted in the methodological reports of the INE.[29] Regardless, there is no indication that these limitations would significantly affect the quality of the data and the results obtained from their analysis.

In addition, because the mortality data obtained from the INE do not provide individual data on CVRFs or on treatments or lifestyles, our analysis could not consider these variables. Accordingly, the reasons mentioned in the discussion of the present study to explain the observed mortality patterns were based on the literature consulted and were analyzed in the current work.

CONCLUSIONS

By analyzing the rate of PM due to IHD in the entire Spanish territory, our results show that there was a continued and marked tendency for a decrease in PM in both sexes during the study period. Both AAMRs of mortality and its variations were not

homogeneous throughout the country but the heterogeneity was reduced at the end of the period, which suggests that the interprovincial differences are being dampened in recent years.

ACKNOWLEDGMENTS

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CONFLICTS OF INTEREST

The authors have no conflicts of interest to declare.

WHAT IS KNOWN ABOUT THE TOPIC?

- Mortality due to IHD is very high. National AAMRs of mortality have decreased in men and women for several decades, although studies have not found significant differences at regional levels. A heterogeneous geographical distribution is evident, with higher mortality in southern and eastern Spain.

WHAT DOES THIS STUDY ADD?

- The AAMRs of premature mortality continue to fall, significantly so in all provinces and in both sexes. The north-south divide is being softened, as in other studies of diabetes and CVRFs. The current data do not permit separate quantification of the effects of CVRF prevention, treatments, or implementation of the Infarction Code Program and catheterization units.

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.2020.09.034

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