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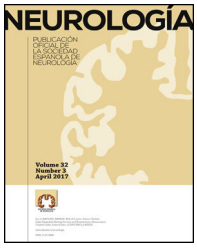

ORIGINAL ARTICLE

Analysis of cerebrovascular disease mortality trends in Andalusia (1980—2014)☆

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KEYWORDS
Regression analysis;
Cerebrovascular diseases;
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Abstract
Introduction: In recent decades, mortality rates for cerebrovascular diseases (CVD) have decreased significantly in many countries. This study analyses recent tendencies in CVD mortality rates in Andalusia (1980-2014) to identify any changes in previously observed sex and age trends.
Patients and methods: CVD mortality and population data were obtained from Spain's National Statistics Institute database. We calculated age-specific and age-standardised mortality rates using the direct method (European standard population). Joinpoint regression analysis was used to estimate the annual percentage change in rates and identify significant changes in mortality trends. We also estimated rate ratios between Andalusia and Spain.
Results: Standardised rates for both males and females showed 3 periods in joinpoint regression analysis: an initial period of significant decline (1980-1997), a period of rate stabilisation (1997-2003), and another period of significant decline (2003-2014).
Conclusions: Between 1997 and 2003, age-standardised rates stabilised in Andalusia but continued to decrease in Spain as a whole. This increased in the gap between CVD mortality rates in Andalusia and Spain for both sexes and most age groups.

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PALABRAS CLAVE
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Análisis de las tendencias en la mortalidad por enfermedades cerebrovasculares en Andalucía (1980—2014)

Resumen
Introducción: En las últimas décadas las tasas de mortalidad por enfermedades cerebrovasculares (ECV) han descendido de forma importante en muchos países. En este estudio se analizan los cambios recientes en la evolución de la mortalidad por ECV en Andalucía (1980-2014) para verificar si las tendencias observadas previamente por sexo y grupos de edad continúan.
Pacientes y métodos: Los datos de mortalidad por ECV y las poblaciones necesarias para el cálculo de los indicadores fueron facilitados por el Instituto Nacional de Estadística. Se calcularon las tasas específicas por grupos de edad y estandarizadas mediante el método directo (población estándar europea). Mediante análisis de regresión «joinpoint» estimamos el porcentaje de cambio anual de las tasas e identificamos puntos de cambio significativos en la tendencia. Además se han estimado las razones de tasas entre Andalucía y España.
Resultados: Las tasas estandarizadas en ambos sexos muestran en el análisis joinpoint 3 periodos: un periodo inicial de descenso significativo (1980-1997), un periodo de estabilización en las tasas (1997-2003) y un periodo de marcado descenso significativo (2003-2014).
Conclusiones: En el periodo 1997-2003 las tasas de Andalucía se estabilizaron, mientras que a nivel nacional las tasas continuaron descendiendo. Esto determinó un aumento en la brecha entre las tasas de Andalucía y España en ambos sexos y en la mayoría de los grupos de edad.

Introduction

Although cerebrovascular disease (CVD) mortality rates have considerably decreased in many countries,[1] CVDs still constitute the third greatest cause of death[2] and the second leading cause of disability worldwide.[3]

Social inequalities in health are unjust, avoidable differences between population groups as defined in terms of social, economic, demographic, or geographical characteristics. These inequalities result from uneven access to healthcare opportunities and resources due to differences in social class, sex, geographical location, or ethnicity, which results in poorer health among socially disadvantaged populations.[4]

The incidence[5] and mortality[6] of CVDs are higher among socioeconomically disadvantaged people. Despite extensive evidence of social disparities in CVD survival, the causes are yet to be fully understood.[7,8] According to a recent review article,[9] CVDs disproportionately affect low- and middle-income countries; furthermore, differences between these and high-income countries have increased.[10]

Although CVD mortality has been observed to have decreased considerably in Spain over the 1980 to 2011 period,[11] marked geographical differences are still observable (rates have remained constant or have decreased to a lesser extent in some areas of southern Spain).[12]

In a previous article, we analysed CVD mortality trends in Andalusia (1975-1999)[13] and reported a marked decrease, regardless of sex. In this study, we provide updated information, analyse changes in CVD mortality in Andalusia, and determine CVD mortality trends by sex and age group for the period 1980 to 2014, and compare these data to data drawn from the population of Spain as a whole.

Patients and methods

Data on the number of deaths, classified by year of death, sex, and age, were obtained from Spain's National Statistics Institute. Population data for Andalusia and Spain, by sex and age group, were also drawn from Spain's National Statistics Institute for each study year (1980-2014).

CVD deaths were identified with ICD-9 codes 430-438 and ICD-10 codes I60-I69 for the periods 1980 to 1998 and 1999 to 2014, respectively.

We also calculated age-specific crude mortality rates for each sex, which were adjusted for age (European standard population). Rates are expressed as number of deaths per 100 000 person-years.

Trend analysis was performed with joinpoint regression models.[14,15] These models have a double purpose: to identify time points associated with significant changes in trends, and to estimate the magnitude of trend changes in each time period. Results are expressed as the years (period) making up each trend and the annual percentage change (APC) for each trend. To estimate these models, we used standardised mortality rates (SMR) and their standard errors; in models using age-specific rates, we used deaths and populations applying the Poisson distribution. To reduce the likelihood of obtaining trends resulting from random fluctuations, we set a minimum number of 5 data points between 2 joinpoints. We established a maximum of 3 joinpoints for each regression model. The software searches for the simplest model that fits the data using the weighted least-squares technique and estimates statistical significance using the Monte Carlo Permutation method. A comparability test was performed to check whether trends

Table 1 Number of deaths due to cerebrovascular disease and population size, broken down by age group and sex (Andalusia, 1980 and 2014).

	Deaths			Population		
Age (years)	1980	2014	Δ	1980	2014	Δ
Men						
< 40	60	14	−77%	2 103 609	2 123 881	1%
40-44	28	21	−25%	167 867	347 660	107%
45-49	52	33	−37%	191 212	337 100	76%
50-54	76	46	−39%	173 439	300 623	73%
55-59	138	67	−51%	152 262	251 886	65%
60-64	197	104	−47%	109 227	204 275	87%
65-69	408	159	−61%	98 857	186 746	89%
70-74	662	231	−65%	77 711	145 419	87%
75-79	837	369	−56%	50 024	111 935	124%
80-84	608	557	−8%	21 860	85 652	292%
≥ 85	486	781	61%	10 800	55 350	412%
Total	3552	2382	−33%	3 156 869	4 150 526	31%
Women						
< 40	47	12	−74%	2 027 751	2 031 313	0.2%
40-44	13	11	−15%	173 691	337 204	94%
45-49	28	14	−50%	194 516	334 504	72%
50-54	45	21	−53%	180 080	302 136	68%
55-59	102	28	−73%	161 276	257 723	60%
60-64	169	40	−76%	134 385	213 232	59%
65-69	381	73	−81%	127 838	204 216	60%
70-74	709	189	−73%	109 581	169 615	55%
75-79	1117	339	−70%	80 059	148 857	86%
80-84	1139	745	−35%	42 237	129 401	206%
≥ 85	1255	1748	39%	26 004	112 124	331%
Total	5005	3220	−36%	3 257 418	4 240 325	30%

Δ: percentage increase 1980 to 2014.

in men and women or between geographical areas were parallel.[16] Statistical significance was set at $P = .05$.

Results

Table 1 shows the number of deaths and the population of Andalusia by sex and age group for the first and last years of the study period (1980 and 2014), and the percentage change between these 2 years. The number of deaths decreased both in men and in women for all age groups except for individuals aged 85 years or older (61% increase in men and 39% increase in women). Population increased both in men and in women for all age groups, although increases were much more marked among individuals aged 85 years and older (412% increase in men and 331% increase in women).

Fig. 1 shows sex-specific CVD SMRs in Spain and Andalusia for the 1980 to 2014 period, and Fig. 2 shows the Andalusia/Spain SMR ratio. Adjusted CVD SMRs show a marked, steady decrease in both sexes and in both Andalusia and Spain over the study period (Fig. 1).

In Spain, SMRs in men decreased from 146.9 in 1980 to 30.8 in 2014. Joinpoint regression analysis shows 2 distinct periods; both follow a downward trend, which is more marked in the second period (2005-2014, −5.8%, $P < .05$) than in the first (1980-2005, −4.2%, $P < .05$) (Fig. 1). SMRs are slightly lower in women than in men and do not follow a parallel trend. The joinpoint regression model reveals 3 periods where the decrease rate increases significantly: 1980 to 1984, −3.5%; 1984 to 2005, −4.6%; and 2004 to 2014, −5.8% (Fig. 1).

In Andalusia, SMRs for men decreased from 170.6 in 1980 to 42.1 in 2014. Joinpoint regression analysis shows an initial period of significant decreases (1980-1997, −4.0%), a period of relative stability (1997-2003, −1.2%, non-significant), and a third period of significant, marked decreases (2003-2014, −6.0%, $P < .05$) (Fig. 1, Table 2). SMRs are slightly lower in women than in men and do not follow a parallel trend. Over the study period, adjusted rates fell from 149.2 in 1980 to 33.6 in 2014. Joinpoint regression analysis shows an initial period of significant decreases (1980-1997, −4.2%), a period of stability (1997-2003, −1.6%, non-significant), and a third period of significant, marked decreases (2003-2014, −6.6%, $P < .05$) (Fig. 1, Table 3).

Fig. 2 shows how Andalusia/Spain SMR ratios peak in 2005, both for men (1.45) and for women (1.52).

Tables 2 and 3 show the results of the joinpoint regression analysis, that is, the points representing significant changes in rates (age group—specific, crude, and adjusted), and the APC for each trend in Andalusia, for both men and women.

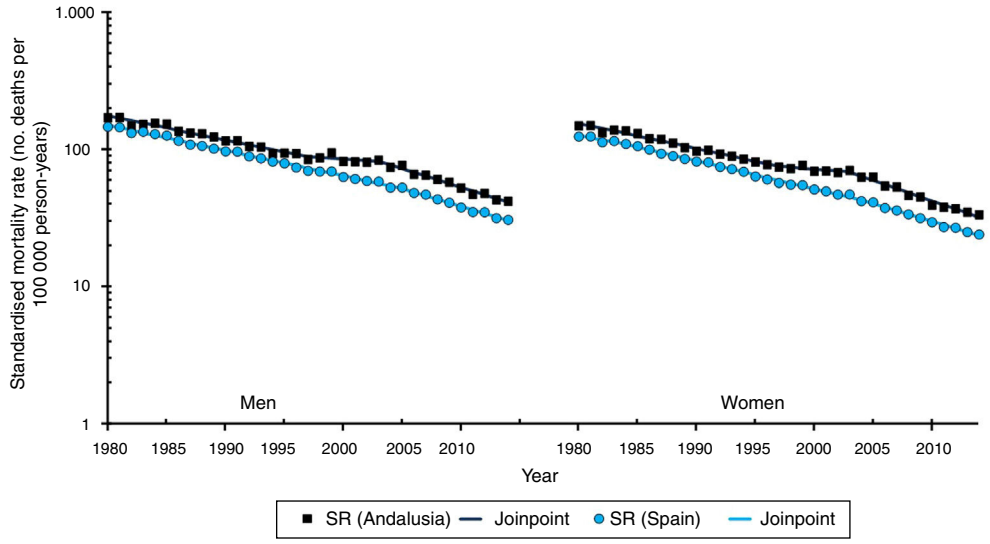

Figure 1 Standardised cerebrovascular disease mortality rates and Andalusia/Spain mortality rate ratio by sex (1980-2014). SR: standardised rate.

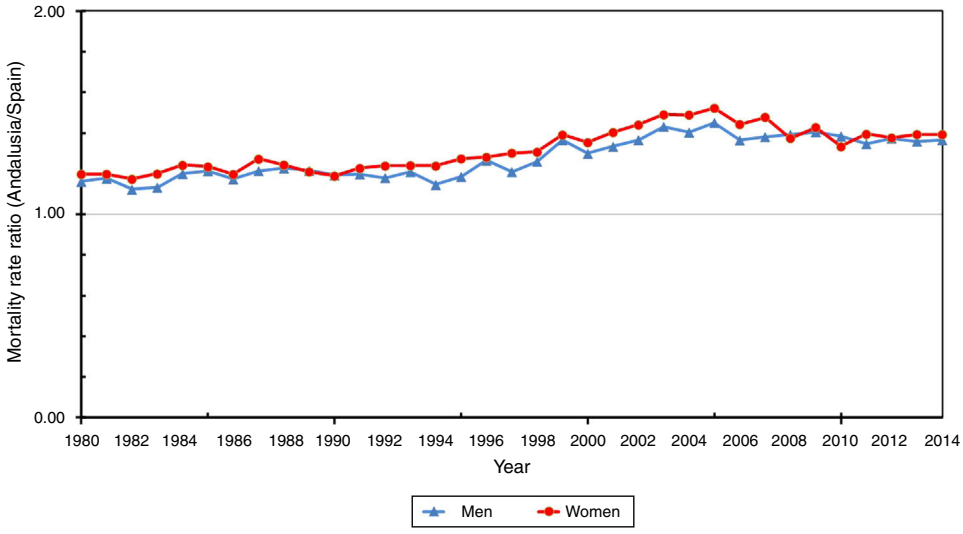

Figure 2 Sex-specific Andalusia/Spain cerebrovascular disease mortality rate ratio (1980-2014).

No joinpoints were observed in the decrease in rates (which ranged from −2.6% to −4.3%) in men aged 40 to 54 years or in women younger than 54 years for the period 1980 to 2014. During the 1990s and the first years of the 21st century, SMRs stabilised or decreased more slowly in men aged 60 to 84 years and in women aged 55 to 59 and 65 to 74 years. After this period, the decrease is more pronounced, both in men and in women.

Fig. 3 shows the age- and sex-specific CVD mortality rate ratios (Andalusia/Spain) for the years 1980 and 2014. In both years, age-specific rates for men in Andalusia are higher than rates in Spain for all age groups except for men aged < 40 years and 50 to 54 years in 1980, and men aged < 40 years in 2014. Differences between rates in Andalusia and Spain increased between 1980 and 2014 in all age groups except for men younger than 40. For women, rates in Andalusia were lower than those in Spain only for the age groups below 55 years in 1980 and the age group 50 to 54 years in 2014. Most age groups showed an increase in the difference between Andalusia and Spain from 1980 to 2014.

Discussion

Studies of mortality due to CVD provide preliminary data on the risk of CVD by age, sex, and geographical location, and estimate case fatality and time trends,[17] especially when incidence data is scarce.[18] Official data on mortality due to CVD may be used for trend analysis and comparisons, at least in those countries where mortality data includes validation of diagnosis.[19]

During the 1990 to 2010 period, CVD mortality rates decreased by 20% in low-income countries and by 37% in high-income countries.[9]

Table 2 Age-specific trends in standardised cerebrovascular disease mortality rates (men, Andalusia 1980-2014).

	Rate		Trend 1		Trend 2		Trend 3		Trend 4	
Age group (years)	1980	2014	Period	APC	Period	APC	Period	APC	Period	APC
< 40	2.9	0.7	1980-1987	3.1	1987-1994	-9.1*	1994-2014	-3.2*		
40-44	16.7	6.0	1980-2014	-3.4*						
45-49	27.2	9.8	1980-2014	-3.3*						
50-54	43.8	15.3	1980-2014	-3.3*						
55-59	90.6	26.6	1980-2014	-3.5*						
60-64	180.4	50.9	1980-1997	-4.8*	1997-2002	0.7	2002-2014	-5.1*		
65-69	412.7	85.1	1980-1990	-6*	1990-2004	-2.4*	2004-2014	-6.6*		
70-74	851.9	158.9	1980-1993	-5.2*	1993-2007	-3.2*	2007-2014	-7.7*		
75-79	1673.2	329.7	1980-1997	-5.0*	1997-2005	-2.0	2005-2014	-6.7*		
80-84	2781.3	650.3	1980-1989	-2.7*	1989-1994	-6.3*	1994-2003	-1.9*	2003-2014	-6.5*
≥ 85	4500.0	1411.0	1980-2004	-2.3*	2004-2014	-6.2*				
CR	112.5	57.4	1980-1995	-2.2*	1995-2003	0.2	2003-2014	-3.7*		
SR	170.6	42.1	1980-1997	-4.0*	1997-2003	-1.2	2003-2014	-6*		

APC: annual percentage change; CR: crude rate; SR: standardised rate.
* $P < .05$.

Table 3 Age-specific trends in standardised cerebrovascular disease mortality rates (women, Andalusia 1980-2014).

	Rate		Trend 1		Trend 2		Trend 3		Trend 4	
Age group (years)	1980	2014	Period	APC	Period	APC	Period	APC	Period	APC
< 40	2.3	0.6	1980-2014	-4.3*						
40-44	7.5	3.3	1980-2014	-2.6*						
45-49	14.4	4.2	1980-2014	-3.8*						
50-54	25.0	7.0	1980-2014	-4.1*						
55-59	63.3	10.9	1980-1998	-6.0*	1998-2003	3.4	2003-2014	-7.2*		
60-64	125.8	18.8	1980-1993	-6.1*	1993-2014	-4.1*				
65-69	298.0	35.8	1980-1999	-6.4*	1999-2002	4.0	2002-2014	-8.0*		
70-74	647.0	111.4	1980-1984	-2.8	1984-1993	-7.6*	1993-2000	2.2	2000-2014	-6.2*
75-79	1395.2	227.7	1980-2000	-4.8*	2000-2003	1.7	2003-2014	-7.1*		
80-84	2696.7	575.7	1980-2003	-3.8*	2003-2014	-6.4*				
≥ 85	4826.2	1559.0	1980-1997	-2.6*	1997-2003	0.5	2003-2014	-6.6*		
CR	153.7	75.9	1980-1997	-1.9*	1997-2003	0.4	2003-2010	-5.2*	2010-2014	-1.5
SR	149.2	33.6	1980-1997	-4.2*	1997-2003	-1.6	2003-2014	-6.6*		

APC: annual percentage change; CR: crude rate; SR: standardised rate.
* $P < .05$.

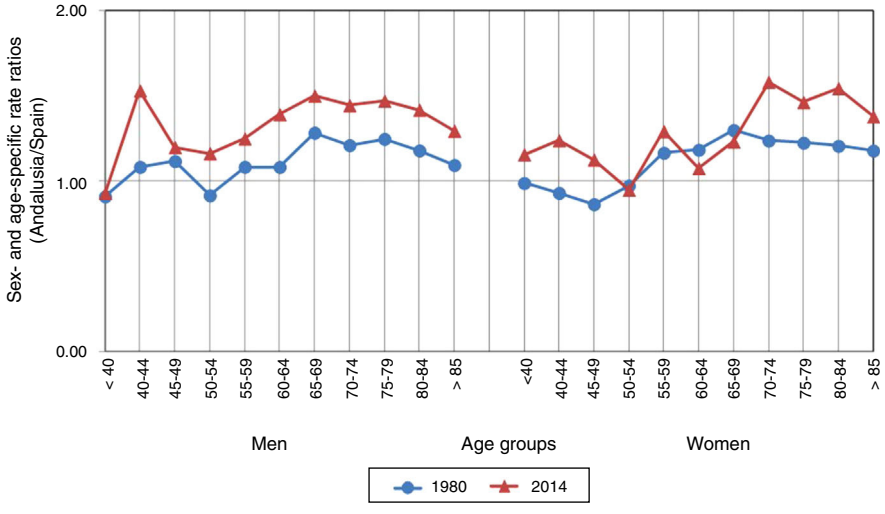

Figure 3 Age- and sex-specific Andalusia/Spain cerebrovascular disease mortality rate ratio (1980 and 2014).

Table 4 Mortality due to cerebrovascular disease in men, by autonomous community (2014).

	Deaths	%	Pop.	%	CR	SR	Rate ratio[a]
Autonomous community							
Andalusia	2382	20.6	4 150 526	18.2	57.4	42.1	2.0
Extremadura	362	3.1	544 067	2.4	66.5	36.5	1.7
La Rioja	110	1.0	155 474	0.7	70.8	33.8	1.6
Asturias	366	3.2	504 565	2.2	72.5	33.6	1.6
Murcia	328	2.8	734 365	3.2	44.7	32.7	1.5
Galicia	939	8.1	1 324 358	5.8	70.9	32.3	1.5
Valencian community	1212	10.5	2 446 996	10.7	49.5	31.5	1.5
Cantabria	165	1.4	286 751	1.3	57.5	30.3	1.4
Aragon	422	3.6	659 321	2.9	64.0	30.0	1.4
Basque country	580	5.0	1 051 770	4.6	55.1	29.7	1.4
Navarre	161	1.4	315 497	1.4	51.0	29.6	1.4
Castile-La Mancha	787	6.8	1 040 531	4.6	75.6	28.7	1.4
Catalonia	1642	14.2	3 630 695	15.9	45.2	27.5	1.3
Castile-Leon	577	5.0	1 229 980	5.4	46.9	26.3	1.2
Balearic Islands	188	1.6	560 645	2.5	33.5	26.1	1.2
Canary Islands	300	2.6	1 054 531	4.6	28.4	23.1	1.1
Madrid	940	8.1	3 063 928	13.4	30.7	21.2	1.0
Ceuta	14	0.1	43 195	0.2	32.4	37.9	1.8
Melilla	24	0.2	42 896	0.2	55.9	70.3	3.3
Spain	11 573	100	22 840 091	100	50.7	30.8	

CR: crude rate; Pop.: population; SR: standardised rate.
[a] Autonomous community/Madrid standardised rate ratio.

The decrease in CVD mortality rates observed in Andalusia for the 1980 to 1997 period is similar to that observed in Spain (−4% per year) and may be attributed to improvements in healthcare for patients with CVDs or CVD risk factors. Reforms in primary care brought about the inclusion of services associated with prevention and care for patients with risk factors[20] (50%-70% of acute strokes are initially assessed by primary care physicians).[21,22] However, other factors must also be involved (factors probably linked to Andalusia's economic and social development in the 1980s): for example, when antihypertensive treatment was introduced, CVD mortality rates were already decreasing.[23]

No appropriate records are available to determine to what extent the decline in mortality is attributable to a decrease in incidence and/or case fatality.

Over the past decades, CVD incidence has decreased by 42% in high-income countries (this has been attributed to preventive treatments and/or a decrease in the incidence of risk factors at the population level), whereas it has multiplied by 2.3 times in low- and middle-income countries.[24]

Estimated incidence in Spain is 120 to 350 cases per 100 000 person-years,[25] although there is considerable variability in terms of geographical locations and time trends. Rates of hospitalisation due to acute CVD have decreased in some areas[26,27] and increased in others.[28,29]

During the 1997 to 2003 period, mortality rates stabilised in Andalusia and decreased in Spain. This results in an increase in the differences between mortality rates in Andalusia and Spain for both sexes and most age groups (Figs. 1-3).

Like Spain as a whole, Andalusia was affected by the economic crisis of the 1990s, coinciding with the worst drought of the 20th century (peaking in 1995), which resulted in disastrous agricultural losses. This socioeconomic situation may have increased the prevalence of risk factors[30] and, despite universal coverage under the Spanish healthcare system, decreased the use of preventive services in socioeconomically disadvantaged populations (which also have greater disease burden)[31]; this may explain a change in CVD mortality trends.[32,33] Furthermore, risk equations based exclusively on clinical factors and used to determine the prescription of preventive treatments underestimate the cardiovascular risk of individuals with a lower socioeconomic level.[34]

The introduction of the ICD-10 in 1999 affected trends of some causes of mortality (rare or non-specific diseases) for the period 1999 to 2004 but had no impact on CVD mortality trends in Spain.[35]

During the 2003 to 2014 period, mortality rates decreased at a slightly faster pace in Andalusia than in Spain as a whole, both in men (−6% vs −5.5%) and in women (−6.6% vs −5.7%). This may reflect the different stroke management strategies in Andalusia: the Integrated Care Process for Cerebrovascular Accidents (2002 and a 2015 revision),[36] the Andalusian Acute Cerebrovascular Disease Plan, establishing code stroke activation and implementing fibrinolytic treatment (2008),[37] and the Andalusian Stroke Care Plan (2011-2014),[38] which may have helped identify and control risk factors.

Andalusia (2014) is one of the most disadvantaged autonomous communities in Spain. It has the highest unemployment rate (34.23%) in the country and the second-lowest per-capita GDP (€16 884) and public healthcare expenditure (€1042).[39] Worldwide, increased unemployment rates and reduced healthcare spending have been associated with a significant increase in mortality due to CVD.[40]

Table 5 Mortality due to cerebrovascular disease in women, by autonomous community (2014).

	Deaths	%	Pop.	%	CR	SR	Rate ratio[a]
Autonomous community							
Andalusia	3220	20.1	4 240 325	18.0	75.9	33.6	2.0
Extremadura	530	3.3	549 741	2.3	96.4	30.5	1.8
Murcia	436	2.7	728 516	3.1	59.8	27.7	1.6
Valencian community	1620	10.1	2 500 350	10.6	64.8	25.7	1.5
Asturias	559	3.5	549 495	2.3	101.7	25.4	1.5
Galicia	1411	8.8	1 414 975	6.0	99.7	24.8	1.5
Castile-La Mancha	1105	6.9	1 027 049	4.3	107.6	24.8	1.5
Cantabria	261	1.6	299 489	1.3	87.1	24.5	1.4
Aragon	586	3.7	669 014	2.8	87.6	24.1	1.4
Balearic Islands	266	1.7	559 825	2.4	47.5	22.3	1.3
Castile-Leon	795	5.0	1 255 355	5.3	63.3	20.8	1.2
Canary Islands	394	2.5	1 063 892	4.5	37.0	20.8	1.2
Catalonia	2233	14.0	3 768 906	16.0	59.2	20.5	1.2
Basque country	726	4.5	1 113 564	4.7	65.2	19.7	1.2
Navarre	198	1.2	320 506	1.4	61.8	19.2	1.1
La Rioja	104	0.6	158 605	0.7	65.6	18.4	1.1
Madrid	1457	9.1	3 312 821	14.0	44.0	16.9	1.0
Ceuta	24	0.1	41 424	0.2	57.9	37.5	1.56
Melilla	16	0.1	41 183	0.2	38.9	32.4	1.34
Spain	16 006	100	23 615 032	100	67.8	24.1	

CR: crude rate; Pop.: population; SR: standardised rate.
[a] Autonomous community/Madrid standardised rate ratio.

The prevalence of risk factors in Andalusia continues to be higher than the Spanish average[41,42] (even surpassing the United States average for obesity and diabetes mellitus)[43]; and CVD mortality rates in Andalusia are the second highest in Spain in both women and men (after Ceuta and Melilla, respectively), and are twice as high as those for the Region of Madrid (which has the lowest rates) (Tables 4 and 5). Furthermore, CVD management (2014) is still lacking, with insufficient equipment and human resources to provide comprehensive, coordinated care (half of Andalusian hospitals lack neurologists and the number of stroke unit beds per 100 000 inhabitants is the lowest in Spain[44]); a lack of specific training in lower-level centres and in primary care; and poor communication between primary and specialised care.[45]

Primary care efforts to control traditional risk factors in socioeconomically disadvantaged populations[46] and ensuring equal access to high-quality acute hospital care are essential to eradicate inequalities in CVD mortality[47] in Andalusia.

Due to population ageing, CVDs continue to pose a challenge for prevention and healthcare policy, especially in elderly populations, in whom prognosis is poorer in terms of both the associated mortality (Table 1) and the functional sequelae and healthcare costs, particularly in the case of cerebral haemorrhages.[48]

Strengths and limitations

We analysed trends in CVD mortality rates over a long period of time (35 years) using joinpoint regression analysis, which can objectively identify periods. This avoids the need for pre-established time periods, which may bias how trends are analysed.

Although our analysis identifies objective changes in CVD mortality rates, the methodology used prevents us from determining the causes of these changes.

Studying mortality rates by year of birth, rather than by age and period, may be more appropriate. In any case, our analysis by age group in consecutive years is reasonably close to this approach.[49]

Conclusions

Our data show that the CVD mortality rate is 50% higher in Andalusia than in Spain as a whole, and twice as high as in the Region of Madrid (the autonomous community with the lowest rate). Although we detected a marked decrease in CVD mortality over the study period (1980-2014), rates stabilised between 1997 and 2003 in Andalusia, whereas they continued to decrease in Spain as a whole, widening the gap between Andalusia and Spain for both sexes and most age groups.

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Conflicts of interest

The authors have no conflicts of interest to declare.

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