Neurología 37 (2022) 550—556

NEUROLOGÍA

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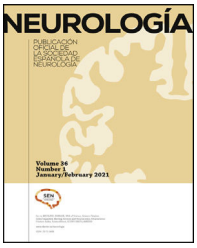

ORIGINAL ARTICLE

Has stroke mortality stopped declining in Spain?☆

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Received 2 May 2018; accepted 20 June 2019
Available online 11 September 2021

KEYWORDS
Cerebrovascular diseases;
Epidemiology;
Mortality;
Trends

Abstract
Objectives: To analyse the changes in stroke mortality trends in Spain by autonomous community and by sex during the period 1980-2016, using joinpoint regression models.
Methods: Mortality data were obtained from the Spanish National Statistics Institute. Crude and standardised rates were calculated for each Spanish autonomous community, and for each sex. Joinpoint analysis was used to identify the best-fitting points showing a statistically significant change in the trend.
Results: Joinpoint analysis enabled us to differentiate between communities in which mortality rates showed a continuous decline throughout the study period in both sexes (Asturias, Cantabria, Castile and Leon, Ceuta, and Melilla) or in men only (Extremadura). In men, in all those communities in which changes in the trend were observed (all but Aragon, the Balearic Islands, and Murcia, where rates remained stable), we observed an initial period of decline (ranging from −3.4% in Catalonia and Extremadura, to −6.0% in Madrid) and a final period where the trends diverged: mortality rates continued to fall in Andalusia, Aragon, the Balearic Islands, and Madrid, but began to stabilise in Castile-La Mancha and Murcia and to increase in the Canary Islands. In women, in those communities where changes were observed (all but Aragon, Murcia, and the Basque Country, where rates remained stable), we observed an initial period of decline (ranging from −3.1% in Catalonia to −6.4% in Navarre) and a final period where divergent trends were observed: rates continued to decline in Andalusia, Aragon, Catalonia, Galicia, Madrid, and the Basque Country, but began to stabilise in Extremadura and Murcia and to increase in the Canary Islands.

☆ Please cite this article as: Cayuela A, Cayuela L, Ortega Belmonte MJ, Rodríguez-Domínguez S, Escudero-Martínez I, González A. ¿Ha dejado de disminuir la mortalidad por enfermedades cerebrovasculares en España? Neurología. 2022;37:550—556.

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Conclusions: Current data show that stroke mortality rates have decreased (in women in Andalusia), stabilised (in both sexes in Murcia, in men in Castile-La Mancha, and in women in Extremadura), and have even reversed (in both sexes in the Canary Islands). Further study is needed to identify the causes of these trends.

PALABRAS CLAVE
Enfermedades cerebrovasculares;
Epidemiología;
Mortalidad;
Tendencias

¿Ha dejado de disminuir la mortalidad por enfermedades cerebrovasculares en España?

Resumen
Objetivos: Analizar los cambios en las tendencias de la mortalidad por enfermedades cerebrovasculares según comunidad autónoma y sexo en España durante el período 1980-2016 utilizando modelos de regresión *joinpoint*.
Métodos: Los datos de mortalidad se obtuvieron del Instituto Nacional de Estadística. Para cada comunidad autónoma y sexo, se calcularon las tasas brutas y estandarizadas. El análisis de regresión joinpoint se utilizó para identificar los puntos más adecuados donde se produjo un cambio estadísticamente significativo en la tendencia.
Resultados: El análisis *joinpoint* permite diferenciar comunidades en las que las tasas muestran un descenso continuado a lo largo de todo el periodo en ambos sexos (Asturias, Cantabria, Castilla y León, Ceuta y Melilla) o sólo en los hombres (Extremadura). En los hombres, en aquellas comunidades en las que se observan cambios en la tendencia se aprecia, en todas ellas (excepto en Aragón, Baleares, y Murcia donde las tasas permanecen estables), un primer periodo de descenso que oscila entre el −3,4% en Cataluña y Extremadura y el −6,0% en Madrid y un periodo final donde las tasas muestran tendencias divergentes: siguen descendiendo en Andalucía, Aragón, Baleares y Madrid, han comenzado a estabilizarse en Castilla-La Mancha y Murcia y aumentan en Canarias. En las mujeres, en aquellas comunidades en las que se observan cambios en la tendencia se aprecia, en todas ellas (excepto en Aragón, Murcia y País Vasco donde las tasas permanecen estables), un primer periodo de descenso que oscila entre el −3,1% en Cataluña y el −6,4% en Navarra y un periodo final donde las tasas muestran tendencias divergentes: siguen descendiendo en Andalucía, Aragón, Cataluña, Galicia, Madrid y País Vasco, han comenzado a estabilizarse en Extremadura y Murcia y aumentan en Canarias.
Conclusiones: Los datos actuales muestran que las tasas de mortalidad por ECV se han desacelerado (en las mujeres de Andalucía), estancado (en ambos sexos en Murcia, en hombres en Castilla-La Mancha y en mujeres en Extremadura) e, incluso, se han revertido (en hombres y mujeres en Canarias). Las causas de estas tendencias requieren más estudios.

Introduction

Cerebrovascular disease (CVD) has long been recognised as an important public health issue. It constitutes the second leading cause of death and the third greatest cause of disability worldwide.[1]

North American countries seem to present considerably lower stroke mortality rates than Europe, where mortality rates vary greatly between countries and regions.[2]

While many countries present consistent decreases in stroke mortality rates,[3] the absolute numbers of deaths, disabled patients, and survivors have increased significantly,[4] and the incidence of stroke is expected to increase in the coming decades as a result of population ageing and increasing prevalence of the main modifiable risk factors.[5]

The dramatic decline in stroke mortality rates observed over the last 4 decades in the United States has slowed, stagnated, and in some cases reverted in recent years, with substantial demographic and geographical differences in the moment and magnitude of the change.[6,7] A similar trend has been described in some European and Asian countries.[8]

In Spain, while mortality rates have decreased since the 1970s,[9] stroke is associated with a considerable disease burden.[10] This decrease accelerated in the 1990s, particularly in older age groups,[11] and has continued into the 21st century,[12] although at different rates in distinct geographical regions.[13]

Since the beginning of the 21st century, joinpoint regression analysis has emerged as a valuable tool for identifying and describing changes in data trends in different time periods,[14] and has been widely used in studies into mortality trends in our setting.[12,13]

In the light of these observations, we designed a study to provide updated information on stroke mortality in Spain and to analyse recent changes (1980-2016) in mortality trends according to autonomous community and sex, using joinpoint regression analysis to verify whether previously existing trends continue to occur.

Patients and methods

Age- and sex-adjusted mortality data were obtained from information published by Spain's National Statistics Institute between 1980 and 2016. We used CVD deaths (codes 430-438 and I60-I69 from the ninth and tenth editions of the International Classification of Diseases [ICD] for the periods 1980-1998 and 1999-2016, respectively) and the populations estimated by Spain's National Statistics Institute as of 1 July of each year in our analysis for the calculation of indicators.

For each autonomous community, we calculated raw and standardised mortality rates for men and women using the direct method, using the European Standard Population as a reference[15]; mortality rates are expressed as deaths per 100 000 person-years.

We analysed trends using joinpoint regression (also known as segmented Poisson regression). These models have a dual purpose: to identify time points associated with significant changes in disease trends, and to estimate the magnitude of trend changes (increases or decreases) for each time period. Results include the years (period) making up each trend and the annual percentage change (APC) for each trend.

We established a minimum of 3 data points between 2 joinpoints. We established a maximum of 3 joinpoints for each regression model. The software fits the simplest model that the data allow using the weighted least-squares technique and estimates statistical significance using the Monte Carlo Permutation method.

To quantify the trend over the entire period, we calculated the average annual percentage change (AAPC) as a weighted geometric mean of APC values from the joinpoint analysis. This measure summarises the trend over the study period. If an AAPC falls entirely within a single segment, the AAPC will be equal to the APC for that segment.

In our description of the results of the trend analysis, the terms ''increase'' and ''decrease'' indicate statistically significant changes ($P < .05$), whereas non-significant results are described as ''stable.''

We used the software's pairwise comparison option to verify whether trends were parallel in each sex.[16] Statistical significance was set at $P = .05$.

All analysis was performed using the Joinpoint Regression software.[17]

Results

Table 1 shows data from each autonomous community on deaths, population, and raw and standardised mortality rates for the years 1980 and 2016, by sex.

Between 1980 and 2016, the number of deaths due to stroke decreased both in men (from 20 304 to 11 556) and in women (from 27 171 to 15 566) in Spain (−43% for both sexes) and in the different autonomous communities (Table 1).

In 2016, Melilla and Andalusia showed the highest standardised rates, both for men (99.6 and 78.5, respectively) and for women (62.2 and 65.6, respectively).

Tables 2 and 3 show the results of the joinpoint regression analysis, indicating the 3 time points at which significant changes occurred and the APC for each trend in men and women in each autonomous community. They also show the AAPC for the study period (1980-2016).

Analysis by autonomous community shows a significant decrease in standardised stroke mortality rates in all regions and for both sexes over the whole study period. Among men, the largest decreases were observed in Ceuta and the Valencian Community (−5.2% in both) and the smallest occurred in Cantabria and Asturias (−3.7% in both). Among women, the largest decrease occurred in the Valencian Community (−5.4%), followed by Ceuta, the Balearic Islands, and Castile-La Mancha (−5.2% in all 3), with Aragon (−3.8%) and Asturias (−4.1%) showing the smallest decreases.

Joinpoint analysis identified the autonomous communities in which the decrease continued throughout the study period, either in both sexes (Asturias, Cantabria, Castile-Leon, Ceuta, and Melilla) or only among men (Extremadura). Among men, all those autonomous communities in which changes in data trend were observed (except Aragon, the Balearic Islands, and Murcia, where rates remained stable) presented an initial period of decreasing mortality (ranging between −3.4% in Catalonia and Extremadura and −6.0% in Madrid) and a final period in which mortality rates showed diverging trends, with rates continuing to decrease in Andalusia, Aragon, the Balearic Islands, and Madrid, beginning to stabilise in Castile-La Mancha and Murcia, and increasing in the Canary Islands.

Among women, all those autonomous communities in which changes in the trend were observed (except Aragon, Murcia, and the Basque Country, where rates remained stable) presented an initial period of decreasing mortality (ranging between −3.1% in Catalonia and −6.4% in Navarre) and a final period in which mortality rates showed diverging trends, with rates continuing to decrease in Andalusia, Aragon, Catalonia, Galicia, Madrid, and the Basque Country, beginning to stabilise in Extremadura and Murcia, and increasing in the Canary Islands.

A comparability test showed that the rates in men and women followed parallel trends in Aragon, the Canary Islands, Ceuta, Madrid, Melilla, Murcia, Navarre, and La Rioja.

Discussion

Our results show considerable differences between regions in stroke mortality rates (with a magnitude approximately double that of the area with lowest mortality for both sexes) and time periods in Spain (1980-2016). These differences may be explained by differences in incidence (reflecting the prevalence and/or control of different risk factors) or in the survival of patients with stroke, or a combination of both factors.[18,19]

The incidence of stroke in Spain is estimated at 120-350 cases per 100 000 person-years, with considerable variations depending on region (higher rates in southern and north-western regions compared to central and Mediterranean regions)[20] and time period (eg, rates of hospitalisation due to stroke have decreased in some areas[21,22] and increased in others).[23,24]

The reasons for the deceleration (in women in Andalusia), stagnation (in both sexes in Murcia, in men in Castile-La Mancha, and in women in Extremadura), or even reversion (in both sexes in the Canary Islands) of the reduction in stroke mortality rates are unclear. These changes may be explained by detrimental changes in the prevalence or control of risk factors, which may have increased the incidence of stroke. The Canary Islands, Extremadura, and Andalusia present the highest prevalence of obesity, diabetes mellitus, arterial hypertension, and dyslipidaemia, in both sexes.[18] Furthermore, the rate of diabetes-related mortality is higher in the Canary Islands than in any other Spanish region.[25]

Hypertension presents a high prevalence in Spain, and is undiagnosed in a considerable percentage of patients with arterial hypertension[26]; although medical treatment is increasingly frequent, the level of control has not improved, and remains low.[27] Furthermore, the increasing prevalence of obesity,[28] diabetes,[29] and smoking, particularly among women,[30] may have contributed to the slowing of the decrease in stroke mortality in recent decades. In addition to these factors, the consequences of the 2008 financial crisis on health and health equity may also be playing a role[31]: some studies have shown that poorer socioeconomic conditions are associated with higher CVD mortality and greater prevalence of CVD risk factors.[32]

Some of the differences in trends between different autonomous communities may be related to differences in the treatment and

Table 1 Cerebrovascular disease mortality according to autonomous community and sex (1980 and 2016).

	Men						Women					
	Deaths		RR		SR		Deaths		RR		SR	
	1980	2016	1980	2016	1980	2016	1980	2016	1980	2016	1980	2016
Andalusia	3552	2341	112.5	56.3	338.7	78.5	5005	3039	153.6	71.5	308.8	65.7
Aragon	734	458	124.0	70.3	238.4	66.6	842	582	139.4	87.5	205.3	50.0
Asturias	510	348	93.2	70.2	225.2	61.7	850	599	146.8	110.7	235.4	56.0
Balearic Islands	431	172	134.8	30.1	304.6	45.3	563	252	171.4	44.1	281.6	42.2
Canary Islands	578	351	85.7	33.0	288.8	47.6	676	453	99.7	42.0	259.0	44.6
Cantabria	213	161	85.1	56.7	209.4	57.3	385	243	147.8	81.7	234.9	48.6
Castile-Leon	1533	821	119.4	68.0	242.7	52.8	1761	1099	134.7	88.9	203.2	42.4
Castile-La Mancha	1259	562	153.7	54.7	313.1	56.1	1573	723	188.2	71.1	295.1	48.1
Catalonia	2856	1538	98.6	42.4	271.8	49.7	4051	2091	134.4	55.2	248.4	39.8
Valencian Community	2720	1238	153.6	50.9	397.6	60.7	3403	1601	184.7	64.2	345.3	51.2
Extremadura	856	309	161.8	57.5	350.7	60.0	1106	515	203.6	94.7	304.4	61.3
Galicia	1789	883	131.8	67.3	301.7	58.2	2745	1369	189.8	97.7	276.1	50.7
Madrid	1337	973	59.7	31.4	194.7	40.7	1837	1389	76.5	41.5	159.5	32.6
Murcia	615	387	132.0	52.6	365.4	76.2	773	473	160.1	64.6	298.0	61.2
Navarre	291	150	115.1	47.4	276.2	51.8	305	192	119.7	59.6	211.7	39.4
Basque Country	781	613	73.9	58.4	250.6	59.5	1000	750	93.0	67.2	200.4	40.8
La Rioja	169	112	133.7	73.2	316.5	71.3	190	97	149.8	61.3	248.7	37.3
Ceuta	26	17	81.5	39.5	337.8	70.0	39	6	117.8	14.4	274.8	19.8
Melilla	16	20	60.9	46.5	182.5	99.6	40	18	145.0	43.2	288.3	62.2
Spain	20 304	11 556	110.4	50.7	291.7	58.6	27 171	15 566	142.3	65.8	257.3	47.9

RR: raw rate; SR: standardised rate (European Standard Population).

Table 2 Joinpoint analysis of cerebrovascular disease mortality in men, by autonomous community (1980–2016).

	Men								
	1980-2016	Trend 1		Trend 2		Trend 3		Trend 4	
Autonomous city/community	AAPC	Period	APC	Period	APC	Period	APC	Period	APC
Andalusia	−4.1*	1980-1997	−3.8*	1997-2003	−1.4	2003-2016	−5.8*		
Aragon	−3.8*	1980-1984	1.2	1984, 1993	−5.5*	1993-2006	−2.4*	2006-2016	−5.8*
Asturias	−3.7*	1980-2016	−3.7*						
Balearic Islands	−5.0*	1980-1985	0.8	1985-1989	−8.5*	1989-2003	−4.2*	2003-2016	−6.9*
Canary Islands	−4.9*	1980-1990	−5.8*	1990-2002	−4.1*	2002-2013	−7.6*	2013-2016	5.8*
Cantabria	−3.7*	1980-2016	−3.7*						
Castile-La Mancha	−4.8*	1980-2003	−4.4*	2003-2011	−7.4*	2011-2016	−2.2		
Castile-Leon	−4.3*	1980-2016	−4.3*						
Catalonia	−4.5*	1980-1990	−3.1*	1990-2016	−5.1*				
Ceuta	−5.2*	1980-2016	−5.2*						
Valencian Community	−5.2*	1980-1993	−4.2*	1993-2016	−5.8*				
Extremadura	−4.7*	1980-2016	−4.7*						
Galicia	−4.6*	1980-2013	−4.2*	2013-2016	−9.3*				
Madrid	−4.5*	1980-1986	−6.0*	1986-1990	0.9	1990-2003	−4.6*	2003-2016	−5.4*
Melilla	−4.4*	1980-2016	−4.4*						
Murcia	−4.3*	1980-1983	0.7	1983-2007	−4.3*	2007-2013	−8.7*	2013-2016	−0.2
Navarre	−4.5*	1980-1989	−6.4*	1989-2016	−3.9*				
Basque Country	−4.2*	1980-1990	−4.6*	1990-2002	−2.7*	2002-2016	−5.1*		
La Rioja	−4.5*	1980-1996	−5.3*	1996-2016	−3.8*				
Spain	−4.5*	1980-2003	−4.1*	2003-2016	−5.3*				

APC: annual percentage change; AAPC: average annual percentage change.
* $P < .05$.

Table 3 Joinpoint analysis of cerebrovascular disease mortality in women, by autonomous community (1980–2016).

	Women								
	1980-2016	Trend 1		Trend 2		Trend 3		Trend 4	
Autonomous city/community	AAPC	Period	APC	Period	APC	Period	APC	Period	APC
Andalusia	−4.3*	1980-1997	−3.9*	1997-2004	−1.8*	2004-2010	−8.0*	2010-2016	−4.4*
Aragon	−3.8*	1980-1984	1.2	1984-1993	−5.5*	1993-2006	−2.4*	2006-2016	−5.8*
Asturias	−4.1*	1980-2016	−4.1*						
Balearic Islands	−5.2*	1980-1998	−4.4*	1998-2016	−6.0*				
Canary Islands	−4.9*	1980-1990	−5.8*	1990-2002	−4.1*	2002-2013	−7.6*	2013-2016	5.8*
Cantabria	−4.2*	1980-2016	−4.2*						
Castile-La Mancha	−5.2*	1980-1992	−3.8*	1992-2016	−5.9*				
Castile-Leon	−4.5*	1980-2016	−4.5*						
Catalonia	−5.0*	1980-1991	−3.4*	1991-1996	−8.0*	1996-2002	−3.8*	2002-2016	−5.7*
Ceuta	−5.2*	1980-2016	−5.2*						
Valencian Community	−5.4*	1980-1993	−4.0*	1993-2016	−6.1*				
Extremadura	−4.3*	1980-1992	−3.4*	1992-2011	−5.6*	2011-2016	−1.5		
Galicia	−4.9*	1980-1999	−4.1*	1999-2008	−6.0*	2008-2012	−1.7	2012-2016	−9.6*
Madrid	−4.5*	1980-1986	−6.0*	1986-1990	0.9	1990-2003	−4.6*	2003-2016	−5.4*
Melilla	−4.4*	1980-2016	−4.4*						
Murcia	−4.3*	1980-1983	0.7	1983-2007	−4.3*	2007-2013	−8.7*	2013-2016	−0.2
Navarre	−4.5*	1980-1989	−6.4*	1989-2016	−3.9*				
Basque Country	−4.3*	1980-1985	−2.1	1985-1989	−7.2*	1989-2002	−3.1*	2002-2016	−5.4*
La Rioja	−4.5*	1980-1996	−5.3*	1996-2016	−3.8*				
Spain	−4.6*	1980-1984	−2.9*	1984-2005	−4.4*	2005-2011	−6.5*	2011-2016	−4.0*

APC: annual percentage change; AAPC: average annual percentage change.
* $P < .05$.

care of patients with CVD, which would lead to differences in case fatality rates.

Since the creation of the Spanish National Health System (with the General Law on Healthcare of 1986) and the transfer of healthcare responsibilities (1981-2001) to the regional health services of the autonomous communities, numerous political, legislative, conceptual, and technical changes affecting public health have been handled differently in each autonomous community, which has led to rich diversity, but also to inequities (the benefits available differ between territories). Thus, despite the existence of the National Health System's stroke strategy (2008) and the implementation of different regional Stroke Care Plans, considerable differences remain between autonomous communities, fundamentally in the availability of technical and human resources.[33,34] Furthermore, few autonomous communities have evaluated these plans' implementation and outcomes; fewer still have published their findings.[35—37]

While intravenous fibrinolysis and code stroke protocols have been broadly implemented, stroke units, specialised neurological care, and reference centres for mechanical thrombectomy are not evenly distributed. Thus, of the 56 established stroke units in Spain as of November 2016, 10 are located in Catalonia, 9 in the Community of Madrid, 6 in the Valencian Community, and 5 in the Basque Country; Extremadura and Castile-La-Mancha only have 2.[38] Furthermore, within the different regional health services, significant differences remain between hospitals in their capacity to respond to new cases of stroke; as a result, place of residence has a greater impact than distance from a healthcare centre in terms of access to appropriate specialised treatment[39] and, therefore, to better prognosis.[40,41]

Strengths and limitations

We conducted a trend analysis of stroke mortality rates over a long period (37 years) by using joinpoint regression analysis, which can objectively identify periods. This avoids the need to use preestablished time periods, which may bias how trends are analysed.

Our study's possible limitations arise from the specific characteristics of the data source (death certificates) and the phenomenon evaluated (mortality). Despite this, the most useful and most widely used tool for assessing the healthcare status of a population continues to be the cause of death recorded on death certificates.[42] Given the limited availability of data on morbidity, mortality is the only universally available indicator in Spain. Problems related to the coding and certification of the cause of death must be taken into account when analysing mortality trends, although the accuracy of this data in Spain is good.[43]

The adoption of the tenth edition of the ICD is unlikely to have had an impact on CVD mortality data, since this category is similar in both of the editions used.[44]

Conclusions

Due to population ageing, CVD continue to represent a challenge for prevention and healthcare policy, especially in elderly populations, who have poorer prognosis in terms of both number of deaths and functional sequelae and healthcare costs, especially in the case of intracerebral haemorrhages[45]; therefore, it would be beneficial to analyse mortality in this age group.

Current data show that the decrease in CVD mortality has slowed (in women in Andalusia), stagnated (in both sexes in Murcia, in men in Castile-La Mancha, and in women in Extremadura), and even reverted (in both sexes in the Canary Islands). Further studies are needed to identify the causes of these trends. New stroke care strategies should result not only in decreases in mortality rates and in the number of patients left severely disabled, but also in a decrease of the regional inequities observed.

Funding

This study has received no private or public funding of any kind.

Conflicts of interest

The authors have no conflicts of interest to declare.

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