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Spatio-temporal trends in gastric cancer mortality in Spain: 1975–2008

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ABSTRACT

Aim of the study: There has been a downward trend in gastric cancer mortality worldwide. In Spain, a marked spatial aggregation of areas with excess mortality due to this cause has long been reported. This paper sought to analyse the evolution of gastric cancer mortality risk in Spanish provinces and explore the possible attenuation of the geographical pattern. *Methods*: We studied a series of gastric cancer mortality data by province, year of death, sex and age group using a conditional autoregressive (CAR) model that incorporated space, time and spatio-temporal interactions. *Results*: Gastric cancer mortality risk decreased in all Spanish provinces in both males and females. Overall, decreasing trends were more pronounced during the first years of the study period, largely due to a sharper fall in gastric cancer mortality risk among the older population. Recent decades have witnessed a slowing in the rate of decrease, especially among the younger age groups. In most areas, risk declined at a similar rate, thus serving to maintain interprovincial differences and the persistence of the geographical pattern, though with some differences. The north and northwest provinces were the areas with higher mortality risks in both sexes and age groups over the entire study period. *Concluding statement*: Despite the decline in gastric cancer mortality risk observed for the 50 Spanish provinces studied, geographical differences still persist in Spain, and the cluster of excess mortality in the north-west of the country remains in evidence.

1. Introduction

At one time, gastric cancer was the leading cause of cancer incidence and mortality worldwide. Although gastric cancer rates have been continuously falling in most parts of the world since the middle of the last century, this tumour remains the fourth leading cause of cancer incidence and second cause of cancer mortality, accounting for 7.8% of all newly diagnosed cancer cases and 9.7% of all cancer deaths respectively [1].

One of the characteristics of gastric cancer epidemiology is its geographical variability. Mortality and incidence rates display remarkable differences among regions; globally, the highest incidence rates are observed in Eastern Asia, and the lowest in Africa and Northern America [1], with more than 70% of cases occurring in developing countries. There are also important regional differences within each continent. In Europe, Belarus is estimated to have the highest gastric cancer incidence and mortality rates, with rates among men being 7-fold those of Sweden; in women, the highest rates are registered in Albania, with incidence rates seven times higher than those of Iceland, and mortality rates 8 times those of Switzerland, France or Cyprus [2].

Although the causes of the decline in gastric cancer incidence and mortality rates are not fully understood, both the marked temporal trends and the geographic variation suggest that environmental and lifestyle factors are strongly implicated in the carcinogenesis of this tumour. The twin discovery of *Helicobacter pylori* (*H. pylori*) [3] in 1983 and its implication in gastric cancer carcinogenesis in 1994 [4] entirely changed the understanding of this cancer's aetiology. Currently, the decline in gastric cancer is attributed to improved living standards, which coincide in time with the widespread use of antibiotics; both factors may have reduced *H. pylori* infection prevalence and incidence rates, and consequently delayed the age of infection. Other accepted risk factors which modulate stomach cancer development are genetics, smoking and diet [5].

Gastric cancer incidence and mortality rates in Spain are not only similar to those reported in other Western countries, but have likewise fallen in recent decades [6–8]. In 1984, the first Spanish Cancer Mortality Atlas described the existence of a spatial pattern in this country, which showed that the highest mortality rates

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were to be found in the Autonomous Region of Castile & León and that these were comparable to those observed for top ranking European countries in terms of mortality due to this cause [9]. This pattern, which is similar in both sexes, has persisted over time [10–12], suggesting that the distribution of stomach cancer in Spain could be modulated by long-standing environmental exposures shared by both sexes, including pollutants delivered via diet and drinking water [12].

Recently, several papers have indicated that the observed decline in gastric cancer mortality in Europe and other areas of the world is likely to continue in the future, since it is observed in countries with high as well as low rates, and among middle-aged and young adults of both sexes [13–15]. Other authors, however, report that gastric cancer incidence and mortality rates tend to stabilise, among the younger age groups in particular [16–18].

In this context, the aim of this study was to explore the possible attenuation of the geographical pattern, by analysing the spatio-temporal evolution of gastric cancer mortality risk in Spain by province, sex and age group. For this purpose, spatio-temporal models have been used to enable gastric cancer trends to be simultaneously studied in respect of both magnitudes. Since changes in risks probably occur gradually over space and time, these methods may allow us to better describe and understand changes in disease trends.

2. Materials and methods

2.1. Data source

To account for possible differences in spatio-temporal mortality patterns, stomach cancer deaths for 50 of Spain's 52 provinces (excluding the autonomous city enclaves of Ceuta and Melilla) were analysed by sex and two age groups (35–64 and >64 years) over the period 1975–2008. Data on population and deaths were drawn from records kept by the National Statistics Institute (*Instituto Nacional de Estadística*). Since the study period saw a changeover from the 9th to the 10th revision of the International Classification of Diseases (ICD), code 151 was used for the period 1975–1998 (ICD-9) and code C16 for the period 1999–2008 (ICD-10). By way of reference, Fig. 1 shows the administrative division of Spain into provinces.

2.2. Statistical analysis

Statistical modelling was performed using a spatio-temporal conditional autoregressive (CAR) model for all age groups, 35–64 and >64 years in both sexes. The model included CAR distributions for the spatial, temporal, and the spatio-temporal interaction random effects [19]. This is a space-time interaction model belonging to the class of models described by Knorr-Held [20], that are in fact extensions of the spatial CAR model introduced by Besag et al. [21]. The CAR model is widely used for smoothing risks as it borrows strength from neighbouring areas in space and time, avoiding the problem of high variability of classical measures such as SMRs in small areas. The description of the model is as follows. Consider that the region under study (Spain) is partitioned into non-overlapping areas (here provinces) denoted by $i = 1, \ldots, I$. Suppose that for each province data are available for several years: $t = 1, \ldots, T$. Then, conditional on the relative risks r_{it}, the number of deaths in each area and year, C_{it}, is assumed to follow a Poisson distribution with mean $\mu_{it} = e_{it} r_{it}$, where e_{it} is the number of expected deaths calculated using the Spanish population as the reference population. Specifically, $e_{it} = \sum_j n_{ijt} R_j$, where R_j is the age-specific rate in Spain in the whole period and n_{ijt} is the population at risk in area i, age group j, and time t. Note that we are standardising by age, considering 5-year age-groups within each

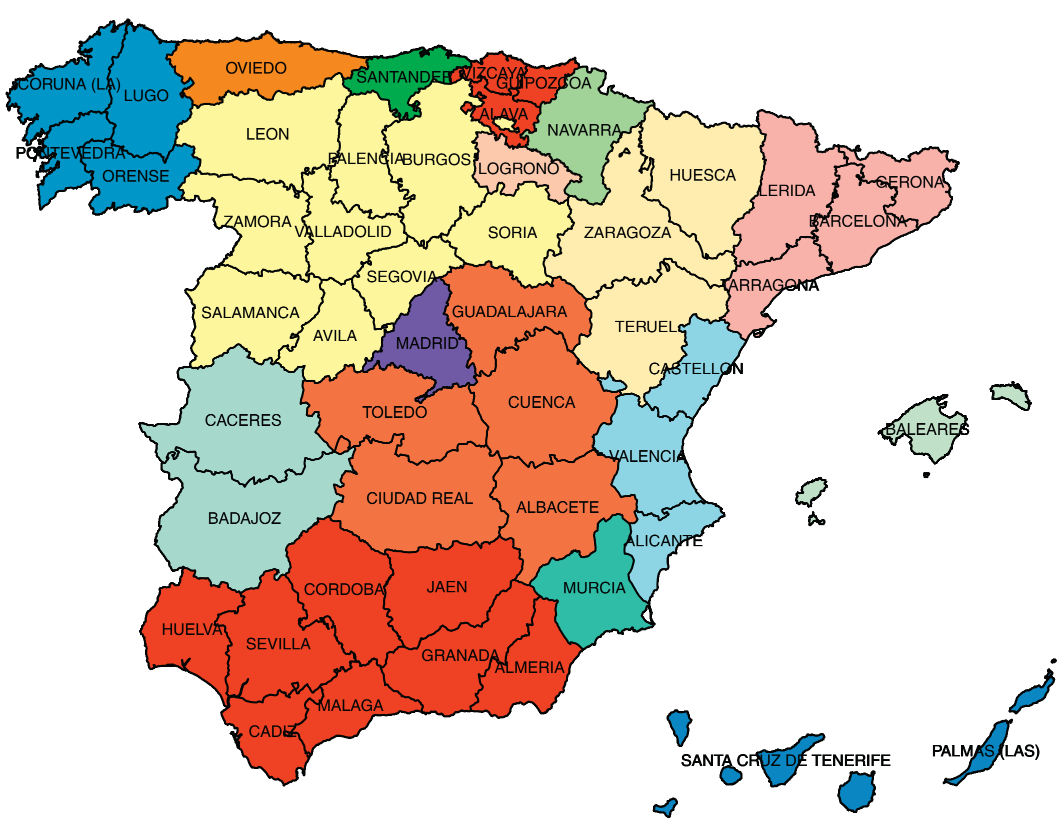

Fig. 1. Administrative division of Spain into provinces. Provinces belonging to the same Autonomous Region share the same colour. Note that the location of the Canary Islands is shown in an inset at bottom right.