Breast cancer mortality trends and patterns in Córdoba, Argentina in the period 1986–2006

Camila Niclis[a], María del Pilar Díaz[b] and Carlo La Vecchia[c]

To estimate the mortality trends and spatial patterns for breast cancer in Córdoba (Argentina) in the period 1986–2006 taking into account age, calendar year, and birth cohort effects. Mortality data were provided by the Department of Statistics, Ministry of Health of Córdoba. Time trends in breast cancer mortality were analyzed using joinpoint analysis and age–period–cohort models. A random-intercept log–linear model was also used to assess the spatial pattern. Breast cancer age standardized mortality rates rose by 1.4% (95% confidence interval 0.2–2.6) per year from 1986 to 1997, and thereafter both breast and total cancer rates declined [−2.5% (−4 to −1.0) and −1.6% (−2.3 to −0.8), respectively]. In age-specific analysis the decline was mainly at age 20–49 years [−2.4% (−4 to −0.9)]. Rates over most recent calendar years decreased, mainly in the most urbanized districts. Age–period–cohort models for Córdoba province and Córdoba Capital showed a favorable cohort effect for generations born after 1955. A decreasing trend in breast cancer mortality was found in Córdoba, especially at younger ages and in most urbanized areas. This could be attributed to some unidentified favorable factors in generations born after 1955. ***European Journal of Cancer Prevention*** **19:94–99 © 2010 Wolters Kluwer Health | Lippincott Williams & Wilkins.**

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[a]Faculty of Medical Sciences, Institute of Cellular Biology, [b]Statistics and Biostatistics Unit, School of Nutrition, Faculty of Medical Sciences, University of Córdoba, Córdoba, Argentina and [c]'Mario Negri' Institute for Pharmacological Research and Institute of Medical Statistics, University of Milan, Milan, Italy

Correspondence to Dr Carlo La Vecchia, MD, Department of Epidemiology, Istituto di Ricerche Farmacologiche 'Mario Negri', Via Giuseppe La Masa, 19, 20156, Milan, Italy
Tel: +39 02 39014527; fax: +39 02 33200231; e-mail: lavecchia@marionegri.it

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Introduction

Breast cancer is the most common cancer in women worldwide. There are more than a million new breast cancer cases each year, resulting in over 400 000 deaths (Ferlay *et al.*, 2004; Parkin *et al.*, 2005). It is the most common cause of cancer death in women in Argentina as well (Argentina, 2006). Breast cancer remains more common in high-income countries, but has been increasing in middle-income and low-income countries, including Latin America (World Cancer Research Fund/American Institute for Cancer Research, 2007; IARC, 2008).

Incidence data are very limited in Argentina. A breast cancer incidence of 44.51 per 100 000 inhabitants was reported in Córdoba province (CP) in 2004 (Díaz *et al.*, 2009), which is currently the only value available from a regional cancer registry from Argentina. However, the Córdoba Cancer Registry is too recent to analyze incidence trends. The scarce information about cancer incidence in our country constrains the study of the disease trends only to mortality statistics series.

Loria *et al.* reported an upward trend (1.06% per year) in breast cancer mortality rates from 1980 to 2003 in CP (Loria *et al.*, 2007). Although trends in mortality rates were stable in Argentina as a whole from 1970 to 2000, Argentina still had the highest value among 10 Latin American countries providing data (Argentina, Brazil, Chile, Colombia, Costa Rica, Cuba, Ecuador, México, Puerto Rico, and Venezuela) at the end of the period (Bosetti *et al.*, 2005).

Mortality patterns may reflect a combination of several factors, including advancements in screening and treatment (American Cancer Society, 2007). With the advent of mammography, there was an increase in early diagnosis of breast cancer, and this led to improved prognosis and survival. In Argentina, only for the last 20 years has the image quality been optimized to the detection of small lesions. Screening methods have raised awareness of breast cancer and have resulted in detecting tumors at an earlier stage, but not all of these have been linked to reductions in mortality (Wilson *et al.*, 2004).

Breast cancer is strongly linked to social and cultural factors that change over time, such as urbanization (Hall *et al.*, 2005) and dietary factors (World Cancer Research Fund/American Institute for Cancer Research, 2007). Diet generally differs by region, mainly between urban and rural areas (Popkin, 2004). It is therefore interesting to analyze time trends and geographical distribution in breast cancer mortality.

This work analyzes the cancer mortality pattern using data from CP. Our aim was to estimate trends over time in breast and total cancer mortality in females in 1986–2006

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by means of joinpoint regression and age–period–cohort (APC) models, and to describe the spatial distribution of breast cancer mortality in the state. The latter approach takes into account time in three ways: age, calendar year, and birth cohort, and allows helpful information to be obtained about age-effect, calendar period-related factors with a short-term influence on all age groups at the same time, and other factors associated with generational exposure to risk factors early in life (cohort effect).

Materials and methods

Breast (and all-cancer) mortality data in 1986–2006 were obtained from the Ministry of Health of Córdoba, Argentina. Classification of cancer deaths was coded according to the Tenth Revision of the International Classification of Diseases (WHO, 2005).

Data on the resident population of CP were obtained from the 1980, 1991, and 2001 censuses available at the National Institute of Statistics and Census. Intercensus population estimates were derived by linear interpolation between two adjacent records for each of the 15 age groups considered. Córdoba is a central Argentinean province with a population of about 3 100 000 inhabitants (9% of the total Argentinean population), which is organized into 26 geographical and urban areas called departments. Its capital, Córdoba city (CC), is the most populated department in the province (about 1 300 000 inhabitants) and the second largest city in Argentina. Overall 80% of the CP population is urban, having 30% of the counties with 100 000–200 000 inhabitant's and only two counties with fewer than 5000 inhabitants in the north of the province. The lower population density is located in this area, and the rural zones cover almost all the south of the province.

Breast and total cancer rates were calculated in three different age groups (20–49, 50–69, and 70–79 years), were age-standardized using the direct method (based on world standard population) and were expressed as rates/100 000. Rates were calculated for CP (overall rate) and for all the geographical and urban areas.

The Joinpoint Regression Program provided by the United States National Cancer Institute was used to estimate the annual percentage changes (EAPC) in mortality rates and its 95% confidence intervals, detecting the number and locations of points at which trends significantly change (Kim *et al.*, 2000; Joinpoint Regression Program, 2008).

To investigate changes in the spatial pattern of the mortality rates, a random intercept log–linear model was used. It allows for heterogeneity between departments (ψ^1) as a level-1 variance, making a simple hierarchical structure to describe the aggregation reported by Díaz *et al.* (2009). Time was included in the model as a factor, considering three levels: initial, middle, and end time points.

In addition, we applied APC models. Data were tabulated into three 5-year (1986–1990 to 1996–2000) and one 6-year (2001–2006) periods of death and 16 overlapping 5-year birth cohorts, identified by central year of birth from 1901 to 1986. For example, the 1941 cohort related to individuals aged 55–59 who died in 1996–1999. The effects of age, period of death, and birth cohort were estimated by using a Poisson regression model (Clayton and Schifflers, 1987) fitted sequentially (Carstensen, 2007). Age–cohort or age–period models are fitted by omitting an explicit intercept and choosing a suitable reference for the cohort (period). The age effect is represented by the log incidence mortality rates for the reference cohort (period) and the cohort (period) effect by the log relative risks relative to this. After that, the log of the fitted values from these models is used as an offset variable in a model with period (cohort) effect, so that the estimates become the age–cohort (period) marginal and period (cohort) effects conditional on the estimates from the age–cohort (age–period) model. We chose a parameterization of our models on the basis of criteria of biological plausibility, namely: age is the major time scale, cohort is the secondary time scale (the major secular trend), and period is the residual time scale. The central year 1941 cohort was chosen as reference cohort.

Data management, direct standardization of rates and Poisson regression analysis were performed using Stata software, version 10 (Stata, 2005).

Results

In CP, breast cancer mortality represents about 20% of all cancer mortality in women in 1986 and 2006. This percentage is even higher (28%) at younger ages (20–49 age group) (Table 1).

Trends in breast and total cancer mortality rates for females at all ages and at ages 20–49, 50–69, and 70–79 years in CP from 1986 to 2006 are illustrated in Fig. 1. Although up to the mid 1990s trends in breast and total cancer at all ages were different, they were similar thereafter. The results of the joinpoint analysis showed that breast cancer age-standardized mortality rates (ASMR) at all ages rose by 1.4% per year from 1986 to 1997, and thereafter both breast and total cancer rates declined (EAPC −2.5 and −1.6%, respectively) (Table 1). It is important to mention the decline (EAPC −2.4%) in breast cancer mortality rates at age 20–49 years since 2000. In addition, the 50–69 years and 70–79 years groups exhibited a fall since mid 1990 (EAPC −2.0 and −1.6%, respectively). Total cancer also declined in all specific age groups.

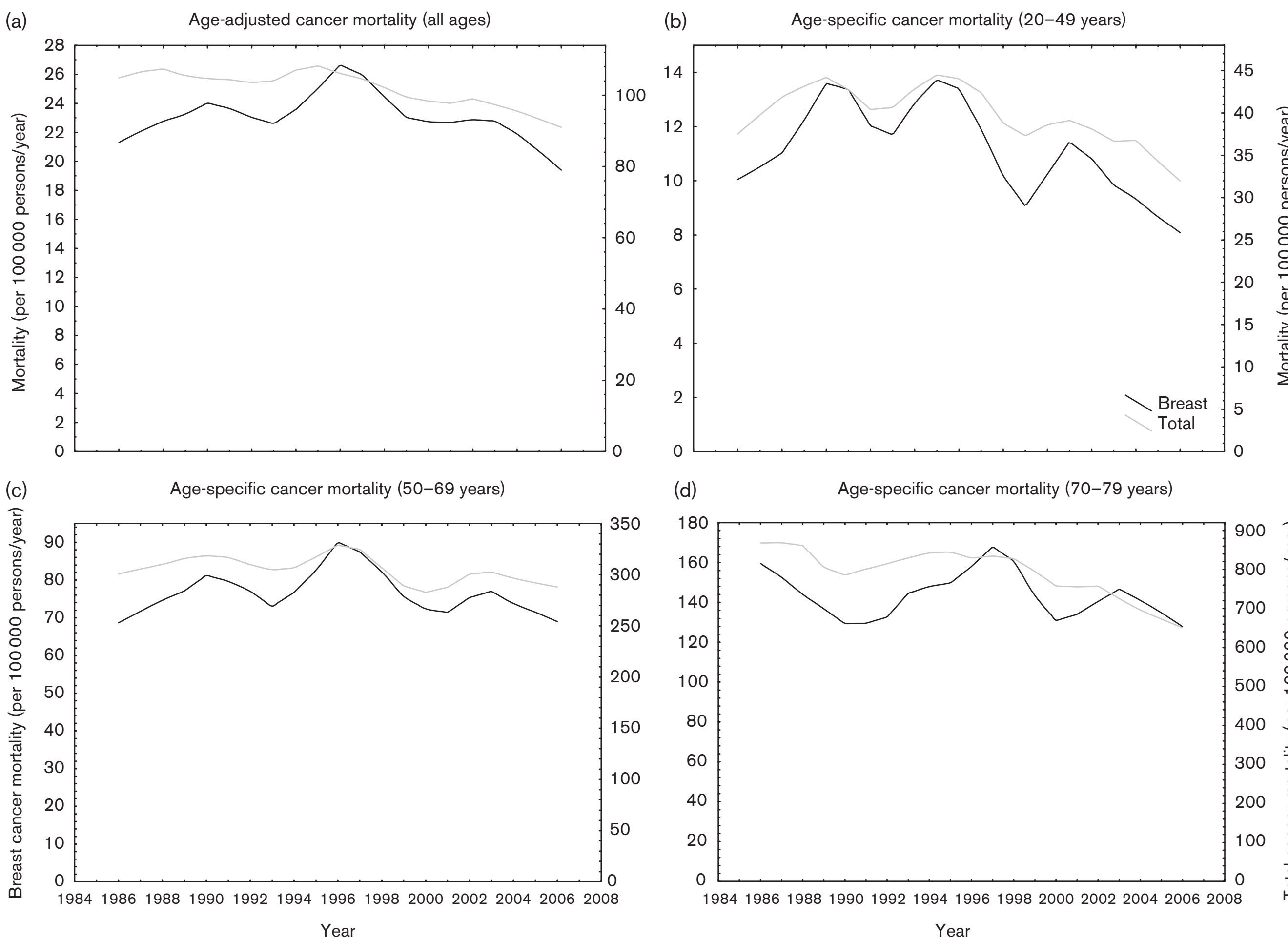
Overall breast cancer rates were 20.9 of 100 000 in 1986, 27.1 of 100 000 in 1997, and 19.6 of 100 000 in 2006. Figure 2 shows the maps of the breast cancer ASMR in CP in the peak year (1997) compared with that from the end time-point (2006). High values were observed, especially in the southern, northeastern, and central

Table 1 Breast cancer and total cancer mortality trends (joinpoint analysis), for females by age group (1986–2006) in Cordoba, Argentina

	ASMR					
	1986	2006	Period	EAPC (95% CI)	Period	EAPC (95% CI)
20–49 years						
Breast	9.9	7.7	1986–1990	10.0 (−3.6 to 26)	1990–2006	−2.4[a] (−4.0 to −0.9)
Total	37.3	3.6	1986–1996	1.0 (−1.1 to 3.1)	1996–2006	−2.3[a] (−3.8 to −0.7)
50–69 years						
Breast	67.6	71.3	1986–1996	1.7 (−0.4 to 3.8)	1996–2006	−2.0 (−4.0 to 0.1)
Total	302.8	288.1	1986–1996	0.3 (−0.7 to 1.3)	1996–2006	−1.0[a] (−2.0 to −0.1)
70–79 years						
Breast	157.2	129	1986–1997	0.9 (−1.2 to 3.0)	1997–2006	−1.6 (−4.0 to 0.9)
Total	844.04	640.9	1986–1998	−0.2 (−1.0 to 0.7)	1999–2006	−2.8[a] (−4.2 to −1.3)
All ages						
Breast	20.9	19.6	1986–1997	1.4[a] (0.2 to 2.6)	1997–2006	−2.5[a] (−4.0 to −1.0)
Total	103.7	90.1	1986–1996	0.2 (−0.6 to 1.0)	1996–2006	−1.6[a] (−2.3 to −0.8)

ASMR, age-standardized mortality rates; CI, confidence interval; EAPC, estimated annual percentage change.
[a]Evidence at 5% level of significance that annual percentage change is greater than or less than zero.

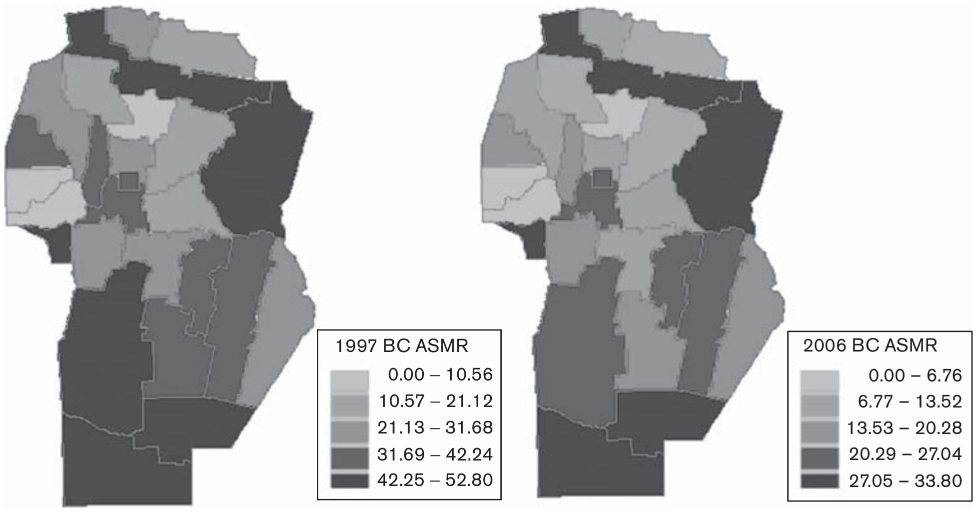
Fig. 1



Breast (left) and total (right) cancer mortality rates for female by age group (1986–2006). Córdoba Province, Argentina, 1986–2006.

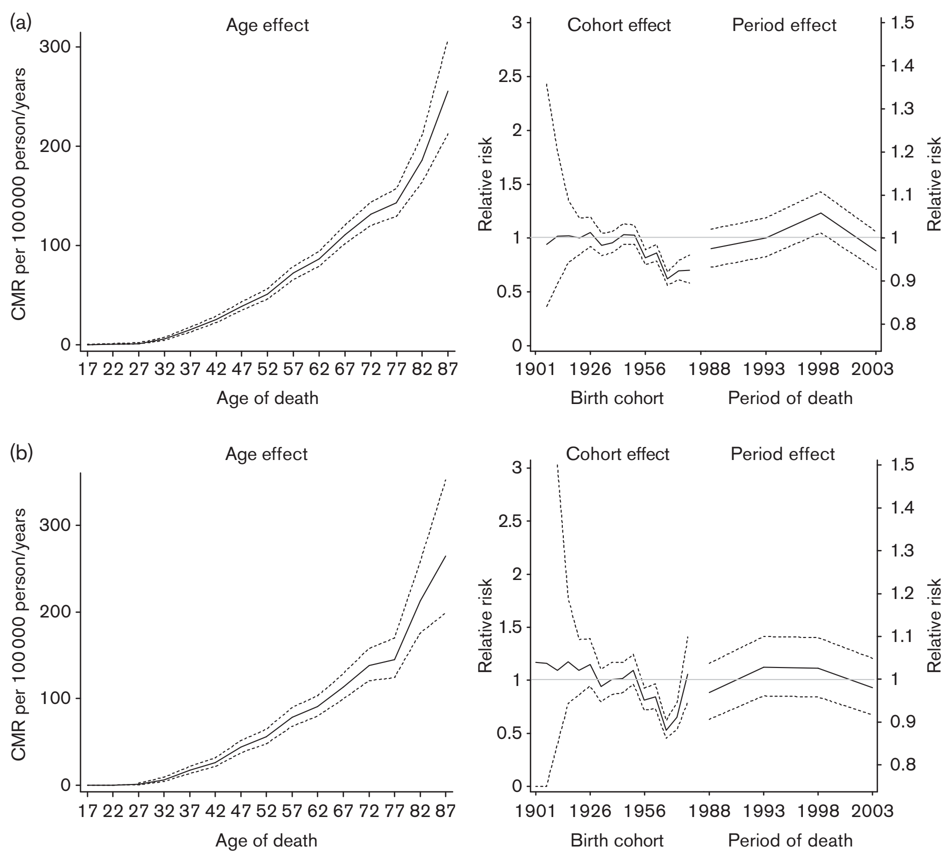
region, including CC (the square), of the province in 1997. Rates in 2006 decreased in those regions, mainly in the most urbanized districts. Similar spatial distributions of mortality rates were identified for time factor (P=0.462, for overall source, P=0.681 for 1997 vs. 2006 moments). Mixed Poisson modeling showed an aggregated pattern, including or not the areas with higher mortality (such as CC, see Fig. 2), indicating that there is no random variability ($(\widehat{\psi}^1) = 1.85$, $SE_{\widehat{\psi}} = 0.249$) between rates.

Fig. 2



Breast cancer ASMR in Córdoba province in 1997 and 2006. ASMR, age standardized mortality rates; BC, breast cancer.

Fig. 3



Breast cancer mortality: age–period–cohort modeling for females. (a) Córdoba province. (b) Córdoba city. Age values are expressed as rates/10^{-5}-person/years. Period of death and cohort of birth effects are expressed in relative terms against their weighted average set to unity. Solid line: effect estimate; dashed line: 95% confidence interval. CMR, cancer mortality rates.

The APC models showed a significant increasing age effect in both the CP and CC breast cancer series (from less than one to more than $250/10^{-5}$-person/year, from 15–20 to 85 or older age groups), with the latter values showing a larger variability (Fig. 3). The curves indicate similar cohort effects in CP and CC with a significantly lower risk of dying from breast cancer in women born in 1956 and 1966. There was only a small effect of period in CC. This effect appeared to be higher for the CP series, with a slight increase in breast cancer mortality risk by the year 1998, and a decline thereafter.

Discussion

We found an increase in breast cancer mortality in Córdoba until the mid 1990s, followed by a decline in breast and total cancer, especially at younger ages (20–49 years). The spatial analysis showed a concentration of high rates in the southern and northeastern region of the province through the years. Furthermore, the APC model showed similar period effects but different cohort effects in the two geographical settings. The coverage level of the Vital Statistics System in Argentina is acceptable (more than 95%) (Loria *et al.*, 2007) and satisfactorily reliable (Muñoz *et al.*, 1998).

Breast cancer is a major public health problem in many countries in South America, and especially in the 'temperate region' (Argentina, Brazil, Uruguay, and Chile), where the incidence and mortality of this disease are comparable to those in most countries in Europe (Schwartsmann, 2001).

In most European countries there has been a continuing fall in breast cancer mortality over the last few years. Overall, such a fall approached 10% between 1995 and 2000, corresponding to a decline of −2.1% per year (Levi *et al.*, 2005). In addition, death rates from breast cancer in women in the USA have decreased since 1990 (Berry *et al.*, 2005). As in Córdoba, the decline was larger among younger age groups. This has been attributed both to improvements in breast cancer treatment and to early detection (Schwartsmann, 2001; Matos *et al.*, 2003), and hence improved diagnosis.

Survival and mortality rates are strongly influenced by the stage at disease presentation (Chilean Society of Mastology, 1999). In Argentina there is no national policy for screening of breast cancer. However, some actions are being taken by nongovernmental organizations to improve the access to screening methods, patient awareness of breast cancer, and to promote the earlier detection of this disease. According to the National Survey of Risk Factors, mammographies were performed in 57.8% of adult women in Córdoba in 2005 (Encuesta Nacional de Factores de Riesgo, 2006) and in 62.3% in Argentina as a whole.

Some recognized risk factors for breast cancer (American Cancer Society, 2007) have not favorably changed over the last years in Argentinean women. For example, there is a delay in age at first full-term pregnancy (the average age rose from 23.2 to 28.1 years over the last few decades) (Lupica and Cogliandro, 2007).

In 2006, although rates in all departments were lower than in 1997, they describe a similar spatial pattern with a larger decrease in most urbanized districts. Highest mortality rates in southern and northeastern regions are inversely related to the socioeconomic development. This may partly reflect differences in access to services for early diagnosis, which are frequently related to most urbanized areas, although there is no information available on this. In addition, the National Survey of Risk Factors showed less physical activity, a possible risk factor for breast cancer (World Cancer Research Fund/American Institute for Cancer Research, 2007), in lower income and less educated populations in CP (Encuesta Nacional de Factores de Riesgo, 2006), and in high mortality rate areas.

APC models make it possible to estimate the effects of age, cohort, and period, which are interesting both for understanding the mechanisms of carcinogenesis and for evaluating the impact of newer diagnostic strategies and therapies on cancer mortality (Levi and La Vecchia, 2002). In fact, a change that affects younger ages may show up several decades later as birth cohort differences in adult mortality (Kuh *et al.*, 2002). There is evidence showing the importance of early life events, including nutrition, physical activity, and factors that affect hormone status, in modification of the risk of breast cancer (World Cancer Research Fund/American Institute for Cancer Research, 2007). The cohort effect curves in CP and CC showed a decreasing trend toward the younger cohorts, with a significantly lower risk of dying from breast cancer in women born in 1956 and 1966, suggesting the presence of some still unidentified favorable factor in those cohorts.

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Conflicts of interest: none declared.

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