# Trends in Breast Cancer Mortality in Spain: It is Really Declined For All Ages Groups?

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**Abstract**

**Introduction**: Incidence in Spain due to breast cancer has increased over the last few years, nevertheless mortality has decreased, especially since 1992. Despite this general decrease in mortality, the intensity has been different in all age groups. The main objective of this paper is to fit the mortality due to breast cancer for different age groups in Spain during 1981-2008, and to forecast for 2023.

**Methods**: Trends in mortality due to breast cancer was carried out with the Lee-Carter model, typical to analyze the mortality in general population but slightly used to analyze a specific cause of death.

**Results**: We found an evident decreasing trend during the last few years of the fit (1993-2008), furthermore we expect a decrease in the mortality due to breast cancer during the years of the forecast. Despite this decrease, the mortality rates have different intensities for each age group. Younger and central ages groups can notice an evident decreasing trend and extend it to forecast, on the other hand, for older age groups the trend in mortality seems to be stable.

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**Conclusions**: Preventive politics in breast cancer should be different according to age of the patient due to their different evolution.

**Keywords : Breast Cancer, Specific age mortality rates, Lee-Carter model**

# 1 Introduction

In Europe breast cancer incidence has increased in all countries with or without national screening programs [3], however despite this increase in the incidence of breast cancer, mortality has decreased by 1.8% annual during period 1997-2006 [9]. This reduction in the rates of mortality such Spain as in Europe has been attributed to mammography screening, implementation of effective hormone treatments and chemotherapy, and progress in radiotherapy and surgery, these innovations have probably contributed to the observed improvements in breast cancer survival in Europe [1], although the contribution of each factor in the mortality improvement is unknown [14, 19]. Studying mortality trends by age groups is of particular interest since any improvement in this mortality may entail great social and economic consequences, especially when developing specific health plans specifically aimed at these age groups.

Age-Specific studies have been demonstrated a valuable utility for analyzing mortality trends by breast cancer. However, although these studies can describe the trend in breast cancer mortality for age group, very few studies perform predictions for each group [6, 13]. The Lee-Carter model [17] widely used by demographers actuaries and statistical to study mortality can be useful for analyzing an specific cause of death such in breast cancer.

There are several research in mortality trends in general population using the Lee-Carter model and their extensions [18, 20, 22, 25], as far as we know, this model has not been used to describe an specific cause of death, the main advantage is to allows to interpret the model parameters in a simple graph, also allows predictions for each age group. In this paper, we employ the Lee-Carter model, with the main objective, to fit and predict mortality by breast cancer in Spain during 1981-2008 period, and carry out projections to 2023.

# 2 Materials and Methods

## 2.1 Patients

Data on population deaths from 1981 to 2008 was obtained from Ministerio de Sanidad y Política Social e Igualdad. We selected all death by Breast Cancer (ICD-10 C50 and ICD-9 174 codes) during period between 1981 and 2008. These data were obtained disaggregated by age-group and year of death, finally we selected 12 age group (25-29, 30-34, 35-39, 40-44,. . ., 80-84).

## 2.2 Lee-Carter Model

The Lee-Carter Model, developed in Lee and Carter (1992)[17], consists in adjusting the following function to the central mortality rates,

$m_{xt} = \exp\left(a_x + b_x k_t + \epsilon_{xt}\right)$

or, its equivalent

$$\ln\left(m_{xt}\right) = a_x + b_x k_t + \epsilon_{xt} \tag{1}$$

In this previous two expressions, the double subscript refers to the age, $x$, and to the year or unit of time, $t$. $a_x$ and $b_x$ are age-dependent parameters and $k_t$ is a specific mortality index for each year or unit of time. The errors $\epsilon_{xt}$, are assumed to be independent, identically distributed $N\left(0, \sigma_\epsilon^2\right)$ random variables, reflect the historical influences age and time specific effects not captured by the model.

In [18], the author points out that nothing ensures that central mortality rates probabilities in equation 1 exceeded the unit. This may be a problem if we are modelising death probabilities that are solved by performing a logit transformation. It is for that reason that we apply this model to logit death probability $q_{xt}$ as Debón et al. (2008) [8],

$$\ln\left(\frac{q_{xt}}{1-q_{xt}}\right) = a_x + b_x k_t + \epsilon_{xt} \tag{2}$$

The LC model is over-parameterised in the sense that the structure is invariant under either of the following parameter transformations

$$\{a_x, b_x, k_t\} \longmapsto \{a_x, b_x/c, ck_t\}$$

$$\{a_x, b_x, k_t\} \longmapsto \{a_x - cb_x, b_x, k_t + c\}$$

$\forall c$ is a solution. In order to avoid this problem and get a single solution Lee and Carter (1992) impose two constraints

$$\sum_{t=t_1}^{t_n} k_t = 0 \quad \text{and} \quad \sum_{x=x_1}^{x_n} b_x = 1.$$

The estimations of the parameters of the model can be carried out following the Lee-Carter's approach, which uses the first term of the singular value decomposition, $SVD$, the method proposed by Currie et al. (2004)[7], which use conditional generalized linear models, $GLM$, or by means of maximum-likelihood estimations, ML, as Brouhns et al. (2002)[4] this approximation, has employed to fit the model.

### 2.2.1 Bootstrap Predictions

The last step of the *Lee-Carter method* consists of finding a model for the mortality rates values, $\{\hat{k}_t\}$, by using *Box-Jenkins methodology* a good model is obtained by means of the expression,

$$\hat{k}_t = p + \hat{k}_{t-1} + u_t.$$

Where $p$ is a constant and $u_t$ a white noise.

The method utilized is as follow. With the observations $(E_{xt}, d_{xt})$, we simulate $N$ Bootstrap samples $(E_{xt}, d^n_{xt}), n = 1, 2, \ldots, N$, where $d^n_{xt}$ are realizations from a Binomial with parameters $(E_{xt}, \dot{q}_{xt})$. $N$ Bootstrap samples, were simulated with the residuals

$$\hat{\epsilon}_{xt} = logit(\dot{q}_{xt}) - logit(\hat{q}_{xt}), \tag{3}$$

Obtained with the original data. Each sample provides an estimations of $logit(\hat{q}_{xt})^n$ from the inverse formula.

$$logit(\hat{q}_{xt})^n = logit(\dot{q}_{xt}) - \hat{\epsilon}^n_{xt},$$

Where $logit(\dot{q}_{xt})$ were obtained from initials observations $(E_{xt}, d_{xt})$. These provided $N$ realizations of $\hat{a}^n_x, \hat{b}^n_x, \hat{k}^n_t$ proyected, that are used to predict $q_{xt}$. The Interval confidence $IC_{95} = [p_{0,025}, p_{0,975}]$ was obtained from $2,5$ and $97,5$ percentiles. The extension of the *Bootstrap* methods to another models and indicators are immediate.

## 3 Results

Figure 1 shows all adjust parameters of the model, parameter $a_x$ is the general profile of the mortality due to breast cancer in Spain during 1981-2006 period, as we can notice, the mortality increasing with the age, this fact is well known. Parameter $b_x$ represents the decreasing speed of death probability at a certain age in response to changes in $k_t$ positive values of $b_x$, indicate that mortality by breast cancer decreases across time. Finally, we can notice there are a change in the trends of the mortality, $k_t$ index shows how mortality is decreasing from 1981 to 1992 and decreasing to the end.

As it has been already mentioned, the last step of Lee-Carter model consists in predicting mortality for future years, in our case 15 years. In order to carry out predictions, we have adjusted a time series to $k_t$ index by Box-Jenkins methodology using the function *auto.arima* implemented in R[23] in the package Forecast developed by Hyndman [15] that automatically provides the best fit of the time series, in our case has been an ARIMA(0,2,0). In Figure 2 we shows predictions for $k_t$ index and their confidence intervals carried out with non-parametric

Bootstrap, the main advantage of Bootstraping technique is that we can collect all sources of variation. As we can see, our model predict an evident decreasing trend during the 15 year prediction.

Predictions for the probabilities of death were obtained by textit non-parametric Bootstrap. For each individual age group we shows in Figure 3, that the decreasing trends are not equal for all age groups, where for higher ages it seems that the trend in mortality has stabilized over the years. However it is in the thick of the central ages and younger ages where there is a evident decreasing trend.

## 4 Discussion

Mortality trends from breast cancer have been widely studied in recent years, showing a clear decreasing trend in mortality. However we missing in one hand age-speciffic analysis as those by Cabanes et al. 2009 [6] or by Yasmeen et al. (2010) [26] that show us what is happening in mortality trends for each age group, and on the other hand an analysis that is capable of making projections for this mortality, this study aims to answer to both questions.

The main finding is that the mortality in Spain by breast cancer decreasing and will be decreasing over the years of the forecast, the results we have exposed, are in same the direction of several authors, who claim that in Spain the change in the mortality by breast cancer occurred in 1992 [27], we observed the same pattern. However, this decreasing in the mortality we must be carefully to analyze, for this reason is so much important an age-specific analysis, for as we have shown the supposed decreasing trend is not so evident for all age groups. For higher ages of the study the trend has stabilized and center and younger ages is decreasing. For this reason, should make specific health plans as specific treatments targeted at higher ages in order to achieve a decreasing in mortality from this type of tumor in these ages.

The overall increase in use of mammography among women younger than 45 years, might have increased the number of early diagnoses and thus improved survival, this fact is reflected in our results with a evident decrease in mortality by breast cancer for women under 50 years. According to the 2006 Spanish National Health Survey, 4% of women aged 25-34 years and 19% aged 35-44 report biennial mammography [21]. In contrast, breast cancer incidence increased in the young cohorts [24], given that they experienced more intensively the striking lifestyle changes occurred in Spanish society in the last decades. A marked decrease of breast cancer mortality is also found in the group aged 45-64 years which, in addition to improved treatments, would also have benefitted from earlier detection of tumours resulting from their inclusion in screening programs [6]. A marked decrease of breast cancer mortality is also found in the group aged 45-64 years which, in addition to improved treatments, would also have benefitted from earlier detection of tumors resulting from their inclusion in screening programs.

Finally, the smallest decrease or even stabilization in mortality trends in ages above 65 is in the same direction that has found in Spain [6]. In the stabilization process must be weight in is the under treatment of older breast cancer patients. Studies have found that increased patient age is associated with decreased guideline concordandce for definitive surgery, adyuvant chemotherapy and adjuvant hormonal therapy, after adjusting for risk factor and tumor characteristics [5, 16, 12]. Under treatment has shown to increase mortality for breast cancer [5].

By using an administrative database, we find inherent and well known shortcomings [10, 11]. The main shortcomings are related to the little and not very specific clinic information contained, especially as regards to the treatments given to the patient, patient´s precedents and risk factors. Another shortcoming is the impossibility of differentiating between a comorbidity and a complication. However, it is important to consider that it is only national registration of death in Spain.

As a future line of work, we face the possibility of incorporating in the model a cohort effect, since it can be very interesting to observe the effect of birth year in trends of mortality from breast cancer in Spain.

To sum up, the trend in breast cancer mortality has been decreasing for all ages groups, however, although the trend remains decreasing, we see a stabilization for higher ages of adjustment.

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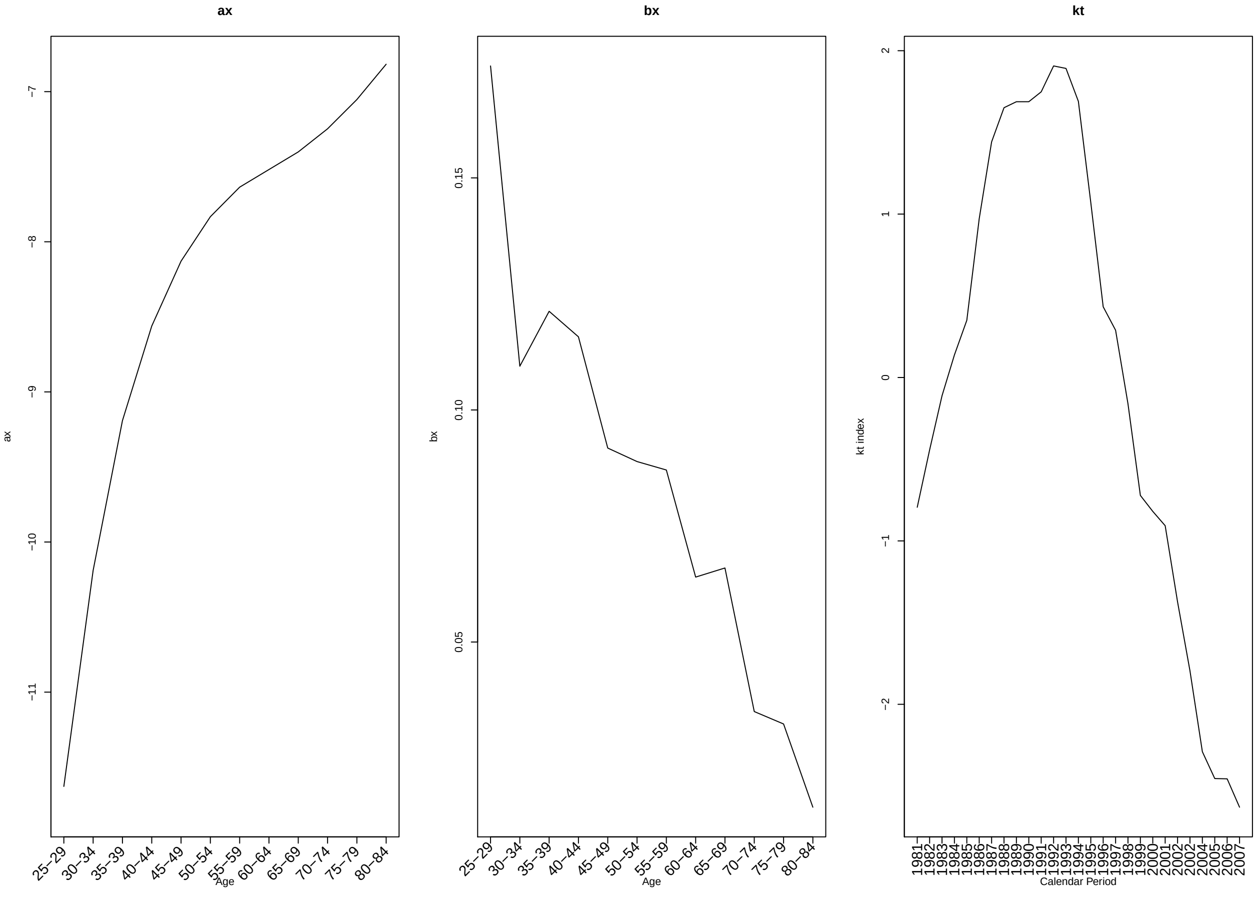


Figure 1: Lee-Carter parameters

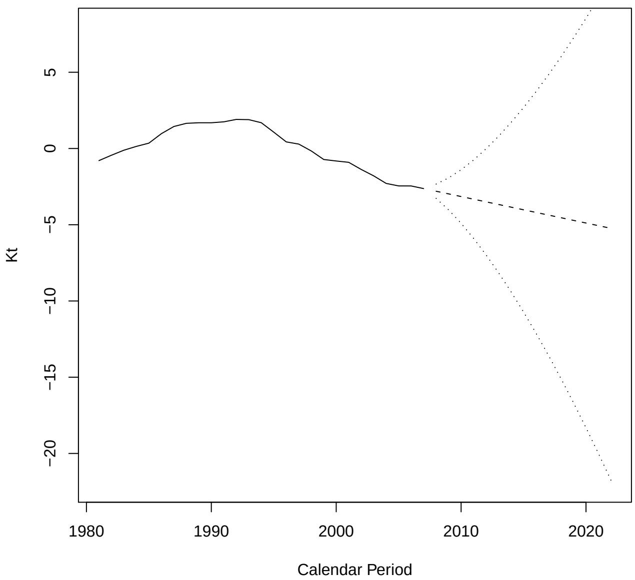


Figure 2: Predictions for $k_t$ index

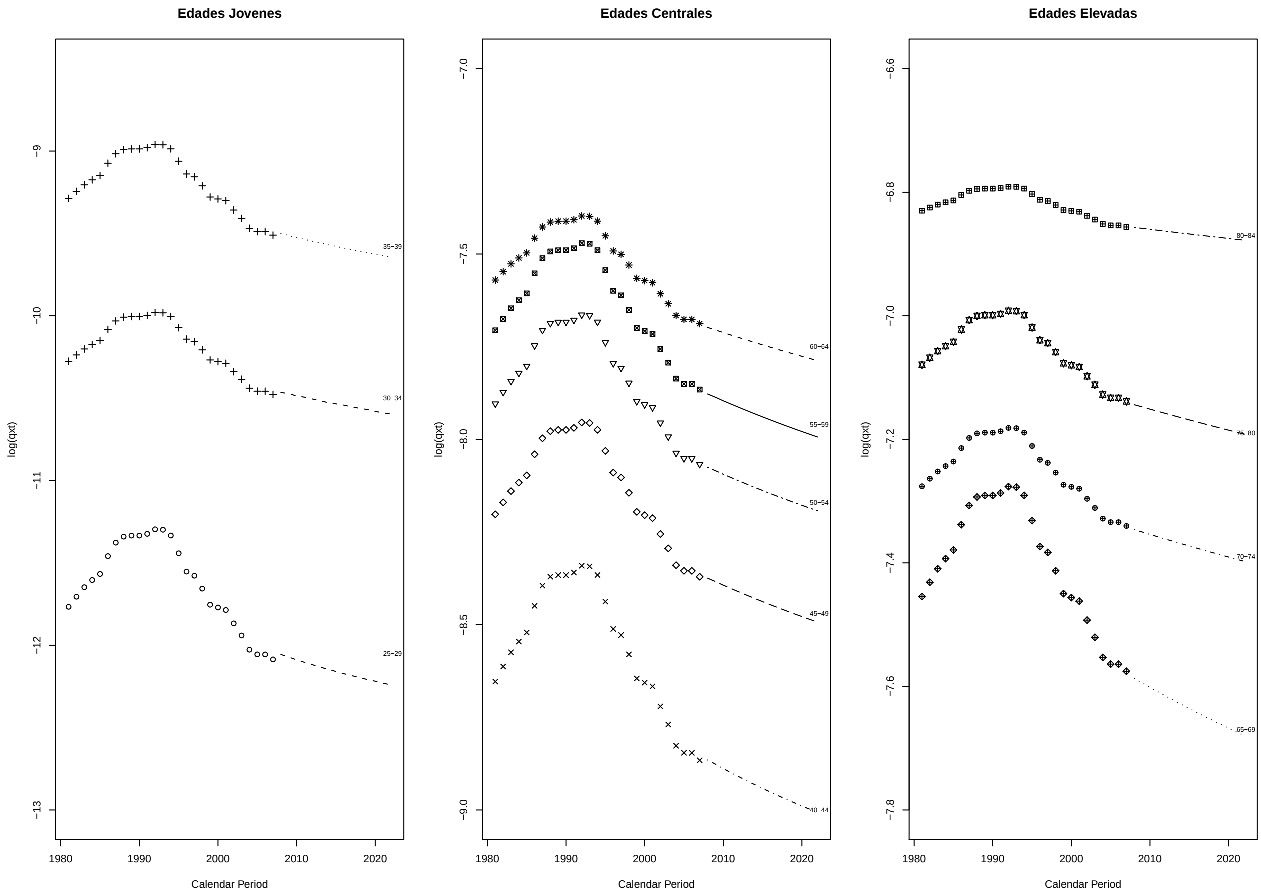


Figure 3: Predictions for the probabilities of death for all age groups