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**CARRERA PROFESIONAL DE MEDICINA HUMANA**

**“EVOLUCIÓN DE LAS TASAS DE MORTALIDAD POR CÁNCER  
DE MAMA EN PAÍSES LATINOAMERICANOS Y SU  
MORTALIDAD PARA EL AÑO 2030”**

Tesis para optar el grado académico de:  
**MAESTRO EN EPIDEMIOLOGÍA Y BIOESTADÍSTICA**

Presentado por:

Junior Smith Torres Roman (0000-0001-5310-6077)

Asesor:

Leda Yamilee Hurtado Roca (0000-0003-1993-6223)

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**ACTA DE SUSTENTACIÓN**

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Presidente: <b>Maestro Franco Ronal Romaní Romaní</b>
Miembro: <b>Maestro Edward Manuel Adriano Mezones Holguín</b>
Miembro: <b>Maestro Juan Jhonnal Alarco Urquizo</b>

Se reúnen para evaluar la tesis titulada: **“EVOLUCION DE LAS TASAS DE MORTALIDAD POR CÁNCER DE MAMA EN PAISES LATINOAMERICANOS Y SU MORTALIDAD PARA EL AÑO 2030”**

Presentada por el Bachiller **Junior Smith Torres Román**

Para optar por el Grado de **Maestro en Epidemiología Clínica y Bioestadística**

Con la asesoría de: **Dra. Leda Yamilée Hurtado Roca**

Luego de haber evaluado el informe final de tesis y evaluado su desempeño en la sustentación, concluyen de manera unánime calificar a:

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*Presidente del Jurado*



**Dra. Leda Yamilée Hurtado Roca**  
*Asesora*



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*Miembro*



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De nuestra consideración,

Yo: Junior Smith Torres Roman, egresado de la carrera de Maestría en Epidemiología y Bioestadística de la Universidad Científica del Sur, en conjunto con la asesora de tesis Leda Yamilee Hurtado Roca, declaramos que este informe final de tesis de investigación titulado: Evolución de las tasas de mortalidad por cáncer de mama en países latinoamericanos y su mortalidad para el año 2030, sustentado para obtener grado de Magister en Epidemiología y Bioestadística es original.

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DNI: 74624844

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Firma del asesor de tesis  
DNI: 40060835

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<sup>14</sup> Los documentos están en: <https://investigacion.cientifica.edu.pe/reglamentos/>

## INFORME DE REVISIÓN DE ORIGINALIDAD

**Título del documento evaluado.** Evolución de las tasas de mortalidad por cáncer de mama en países latinoamericanos y su mortalidad para el año 2030

**Autores.** Junior Smith Torres Roman.

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**Dedicatoria**

Este trabajo va dedicado a mis padres y hermanos, quienes han sido, son y continuarán siendo la fuerza que me impulse en este largo camino de poder ser un notable investigador que ayude a encontrar soluciones para enfermedades crónicas no transmisibles como el cáncer.

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## **Resumen**

### **Antecedentes**

El cáncer de mama es una de las principales causas de mortalidad por cáncer entre las mujeres de América Latina y el Caribe (ALC), pero se carece de un análisis exhaustivo y actualizado de las tendencias de mortalidad. El objetivo de este estudio fue determinar las tasas de mortalidad por cáncer de mama entre 1997 y 2017 para los países de ALC y predecir la mortalidad hasta 2030.

### **Métodos**

Se recuperaron las muertes por cáncer de mama en 17 países de ALC de la base de datos de mortalidad de la Organización Mundial de la Salud. Se estimaron las tasas de mortalidad estandarizadas por edad por 100.000 mujeres-año. Las tendencias de mortalidad se evaluaron con análisis de regresión Joinpoint por país y grupo de edad (todas las edades, <50 años y  $\geq 50$  años). Para 2030, predecimos el número de muertes, las tasas de mortalidad, los cambios en la estructura y el tamaño de la población y el riesgo de muerte por cáncer de mama.

### **Resultados**

Argentina, Uruguay y Venezuela registraron las tasas de mortalidad más elevadas durante todo el periodo de estudio. Guatemala, El Salvador y Nicaragua registraron los mayores aumentos (de 2,4% a 2,8% anual), mientras que Argentina, Chile y Uruguay registraron tendencias a la baja (de -1,0 a -1,6% anual). En mujeres <50y, seis países presentaron tendencias a la baja y cinco países mostraron tendencias al alza. En mujeres  $\geq 50$ y, tres países presentaron tendencias decrecientes y diez mostraron tendencias crecientes. En 2030, se esperan aumentos en la región de América Latina y el Caribe, principalmente en Guatemala (+63,0%), Nicaragua (+47,3), El Salvador (+46,2%), Ecuador (+38,5%) y Venezuela (+29,9%).

### **Conclusión**

Nuestros hallazgos sugieren diferencias considerables en la mortalidad por cáncer de mama en los países de ALC por grupos de edad. Para alcanzar los objetivos de desarrollo sostenible de 2030, los países de ALC deben implementar estrategias de salud pública para reducir la mortalidad por cáncer de mama.

## Abstract

### Background

Breast cancer is among the leading cause of cancer-related mortality among Latin American and Caribbean (LAC) women, but a comprehensive and updated analysis of mortality trends is lacking. The objective of this study was to determine the breast cancer mortality rates between 1997 and 2017 for LAC countries and predict mortality until 2030.

### Methods

We retrieved breast cancer deaths across 17 LAC countries from the World Health Organization mortality database. Age-standardized mortality rates per 100,000 women-years were estimated. Mortality trends were evaluated with Joinpoint regression analyses by country and age group (all ages, <50 years, and  $\geq 50$  years). By 2030, we predict number of deaths, mortality rates, changes in population structure and size, and risk of death from breast cancer.

### Results

Argentina, Uruguay, and Venezuela reported the highest mortality rates throughout the study period. Guatemala, El Salvador, and Nicaragua reported the largest increases (from 2.4% to 2.8% annually), whereas Argentina, Chile, and Uruguay reported downward trends (from  $-1.0$  to  $-1.6\%$  annually). In women <50y, six countries presented downward trends and five countries showed increasing trends. In women  $\geq 50$ y, three countries had decreased trends and ten showed increased trends. In 2030, increases are expected in the Latin America and Caribbean region, mainly in Guatemala (+63.0%), Nicaragua (+47.3), El Salvador (+46.2%), Ecuador (+38.5%) and Venezuela (+29.9%).

### Conclusion

Our findings suggest considerable differences in breast cancer mortality across LAC countries by age group. To achieve the 2030 sustainable developmental goals, LAC countries should implement public health strategies to reduce mortality by breast cancer.

## Introduction

In 2020, breast cancer was one of the most frequently diagnosed and deadliest malignancies in women worldwide, with more than 2 million new cases (24.5% of all cancers) and more than 600,000 deaths (15.5% of all cancers) (1), mainly affecting middle- and low-income countries (2).

Breast cancer is also the most frequent neoplasm among women in Latin America and the Caribbean (LAC) (except in Bolivia) (1, 3), with an increase in both the incidence and mortality rates (1, 4). Since the 1990s, there has been a steady increase in breast cancer mortality rates worldwide, with the highest rates being found in LAC (5). However, the increase in incidence and mortality in LAC has been heterogeneous in the different countries. For example, between 1992 and 2012, Brazil showed an increase in breast cancer mortality, mainly in the age group of 50 to 69 years (6). While in Colombia, in 2018, breast cancer was the leading cause of death from cancer (mortality rate of 10.48 per 100,000 persons) (7). Finally, from 2003 to 2017, the average mortality rate in Peru was 9.97 per 100,000 women (8).

These geographic variations in breast cancer mortality may be due to socioeconomic status, lifestyles, and access to timely care in each country (9-12). Premenopausal women were found to have a higher risk of breast cancer than age-matched postmenopausal women (13-15).

Previous studies in the LAC population have been limited to short periods of time and a limited number of countries, not allowing exhaustive comparison of the evolution of breast cancer trends in this region. In addition, it is important to know how mortality rates have evolved in the last two decades and what patterns will follow in the coming years, with the goal of proposing containment measures for each country in order to reduce mortality by this neoplasm. Therefore, our objective was to provide breast cancer mortality rates between 1997 and 2017 for LAC countries and predict their mortality rates for the year 2030.

## **Materials and Methods**

### **Data source**

We conducted an observational study with an ecological design. The World Health Organization (WHO) mortality database was used, which compiles death registration data from member states and includes information on causes of death. This mortality database is freely accessible at the following link: <https://www.who.int/data/data-collection-tools/who-mortality-database>

Mortality data for LAC countries were extracted for the period from 1997 (or first available year) to 2017 (or latest available year). Breast cancer deaths were identified with the code C50 (ICD-10: malignant neoplasm of the breast). The analysis was performed for 5-year age intervals (0-4, 5-9, 10-14, ..., 85 and over). Projected population estimates for the study countries were obtained from World Population Prospects (16).

### **Age adjusted mortality rates**

We estimated age-standardized mortality rates per 100,000 female-years by the direct method using the Segi world standard population (17). The analysis was performed for 5-year age intervals (0-4, 5-9, 10-14, ..., 85 and older), also divided into two groups, <50 years and  $\geq 50$  years. Age-specific mortality trends were estimated using Poisson models with the Joinpoint regression program version 4.7.0. Joinpoints given by the program were identified and the annual percentage change (APC) and corresponding 95% confidence intervals (95%CI) were estimated for each country. The APC were considered statistically significant with a p-value <0.05. We calculated the average APC (AAPC) for countries that had 2 or more attachment points.

### Predictions of mortality rates

Predictions for the year 2030 were made using the Nordpred package in the R software, based on an age-period-cohort model. An evaluation was made between the last observed period and the last projected period. The predicted data were compared with the expected rate if the rate found for the observed period was maintained in the projected period in each of the age groups evaluated. This evaluation made it possible to identify whether the difference was due to changes in the structure and size of the population or to an increased risk of death from breast cancer, as proposed by Møller et al. using the formula (18):

$$\Delta_{tot} = \Delta_{risk} + \Delta_{pop} = (N_{ff} - N_{off}) + (N_{off} - N_{ooo})$$

Where:

$\Delta_{tot}$ : The total change between the two periods analyzed.

$\Delta_{risk}$ : The change as a function of risk.

$\Delta_{pop}$ : Is the change as a function of changes in population size and structure.

$N_{ooo}$ : The number of observed cases.

$N_{ff}$ : The number of predicted cases.

$N_{off}$ : is the number of expected cases using the rate of the observed period to the population of the last predicted period.

This study was approved by the Institutional Research Ethics Committee of the Universidad Científica del Sur (CIEI-CIENTÍFICA) (449-2021-POS50).

## Results

Figure 1 shows breast cancer mortality rates for the latest available year and their prediction for the year 2030 in LAC countries. In 2017, Argentina (17.5), Uruguay (17.9), and Venezuela (15.6) had the highest mortality rates for all ages, whereas in 2030 Argentina (17.9), Uruguay (15.6), and Venezuela (17.7) will continue to have the highest mortality rates.

Table 1 presents the estimated annual percentage change for age-adjusted mortality rates of breast cancer in LAC countries. Ten countries showed significant increases in their mortality rates: Brazil (+0.5%), Colombia (+1.3%), Ecuador, (+1.4%), El Salvador (+2.4), Guatemala (+2.5%), Mexico (+0.4%), Nicaragua (+2.8%), Panama (+1.2%), Paraguay (+1.8%), and Venezuela (+1.5%), while three countries reported downward trends: Argentina (-1.0%), Chile (-1.6%), and Uruguay (-1.2%) (Figure 2, and Figure 3).

In women under 50 years of age, the mortality rates by breast cancer in Argentina (-0.9%), Costa Rica (-1.6%), Cuba (-1.9%), Mexico (-0.8%), Peru (-1.1%) and Uruguay (-1.8%) significantly decreased, while Brazil (+0.7%), Colombia (+0.5%), El Salvador (+2.2%), Guatemala (+2.2%), and Paraguay (+1.1%) showed significant increases during the study period (Table 2, Figure 2, and Figure 3).

In women aged 50 years and older, mortality rates by breast cancer significantly decreased in Argentina (-1.0%), Chile (-1.7%), and Uruguay (-1.1%) during the study period, while in Brazil (+0.4%), Colombia (+1.4%), Ecuador (+1.7%), El Salvador (+2.6%), Guatemala (+2.7%), Mexico (+1.0%), Nicaragua (+3.3%), Panama (+1.5%), Paraguay (+2.0%), and Venezuela (+1.9%) reported significantly increased. (Table 3, Figure 2, and Figure 3).

According to the predictions for 2030, in women of all ages, most countries showed increases in mortality rates between 2017 and 2030. While decreases in breast mortality rates are predicted in 5 out of 17 countries, increases are predicted for the most Latin American and

Caribbean countries, with the most substantial increases in Guatemala (+63.0%), Nicaragua (+47.3), El Salvador (+46.2%), Ecuador (+38.5%) and Venezuela (+29.9%) ( Table 4).

In women <50 years, the population structure in Cuba and Puerto Rico will decrease by the year 2030, which will positively influence the total change in mortality by breast cancer. Panama will have the greatest increase in population change and change due to risk, which will negatively influence this disease (Supplementary 1). On the other hand, in women  $\geq 50$  years, Cuba will show a decrease in breast cancer mortality, mainly due to a change in its population structure (Supplementary 2).

### **Discussion**

In this study, mortality trends for breast cancer between 1997 and 2017 were compared across LAC countries, and mortality for 2030 was predicted. Certain LAC countries recorded increases in breast cancer death rates of more than 2% annually, while others reported decreases of 1% to 1.6%. Between 1997 and 2027, mortality patterns from breast cancer varied significantly throughout LAC countries depending on the age cutoff of women older and younger than 50 years. The breast cancer mortality rates in Chile, Cuba, Paraguay, Peru, and Puerto Rico are expected to decrease by 2030, although these changes will not be significant.

We found that between 1997 and 2017 Argentina, Uruguay, and Venezuela had the highest breast cancer mortality rates in the region. These results reflect current trends reported by GLOBOCAN for the year 2020, which indicate that these three countries had the highest rates in the region (more than 17 deaths per 100,000) (1, 3). Nevertheless, these rates are low in comparison to countries that have not been included in this study, such as Barbados, Jamaica and Bahamas, which report rates of more than 30 deaths per 100,000 (3).. One of the main risk factors for the development of breast cancer is age, with changes in demographic structure leading to epidemiological changes in which breast cancer will reach epidemic proportions in

LAC. In addition, differences in mortality between countries could be explained by variations in prevention strategies, access to health services, health insurance coverage and patient care practices (i.e., the lack of specialists in the rural areas of each country or specialized institutes for comprehensive cancer management). The inequalities in access to breast cancer care are strikingly visible within the region, and this is evidenced by the mortality outcomes in many of the countries reported in this study.

The disparity in mortality rates between LAC countries for women over and under 50 years old remains significant. When compared to older women, younger women have worse prognoses and a higher risk of breast cancer recurrence and mortality (19, 20). Several studies (21-23) have investigated risk variables that may affect the incidence of breast cancer in different countries. Demographic, socioeconomic, genetic, and lifestyle-related risk variables, as well as reproductive behavior, are the most important risk factors. Age is still the most important factor in the occurrence of breast cancer. Brazil, Colombia, El Salvador, Guatemala, and Paraguay showed significant increases in breast cancer mortality in women under and over 50 years old between 1997 and 2017. As most Latin American countries migrate to a more advanced population age structure, demographic shifts in the region are causing an epidemiological transition. Currently, 6.9% of the Brazilian population is 65 or older, and it is expected to double by 2030, significantly increasing the number of instances of breast cancer. Several studies have investigated the impact of behavioral and lifestyle risk factors on the increased risk of breast cancer (24), such as dietary pattern (25), physical activity (26), smoking (27), and alcohol intake (28). On the contrary, if a very healthy lifestyle is maintained, the chance of getting breast cancer in the premenopausal and postmenopausal stages is reduced by 50% and 80%, respectively (29). The inclusion of mammography screening in primary care programs, as well as the adoption of quality standards, are likely to have played a role in improving diagnoses in



these nations. Women are diagnosed earlier in Brazil, particularly in affluent regions, albeit at a far lower rate than in Sweden. Several LAC studies have found an adverse relationship between the diagnosis of late-stage breast cancer and survival (30-32). Depending on the health organization in each country and individual health insurance, socioeconomic status might influence access to care (including access to early diagnosis and treatment with specific drugs) (33). Access to diagnosis and treatment allows women with breast cancer to be diagnosed at an earlier stage, improving their chances of survival (34). More investment in health systems in LAC countries is required for early detection of breast cancer, earlier diagnosis, and accessible and inexpensive treatment for all women.

Some LAC countries are expected to see reductions in breast cancer mortality rates by 2030. Argentina, Brazil, Paraguay, Uruguay, and Venezuela will have the highest mortality rates in the area, with more than 12 deaths per 100,000 people, while El Salvador and Peru will have the lowest, with less than 6 fatalities per 100,000 people. Our estimations exceed those reported in Los Angeles and Western European countries (37). The limited availability of screening and the time lag between initial suspicion of breast cancer and diagnosis are two characteristics that can affect clinical results, and that inferior access to treatment also has an impact on clinical outcomes (24, 38). Latin American women are diagnosed at a younger age than women in North America and Europe (27). Early menarche, late-term pregnancy, nulliparity, and a lack of nursing are well-known risk factors for breast cancer occurrence (39). Furthermore, lifestyle behaviors such as nutrition and obesity, as well as environmental variables, may contribute to adverse trends in young women (39). To improve future outcomes, programs must be structured, and new interventions welcomed.

This study presents the usual limitations of a cancer registry analysis of a secondary database, such as the quality and validity of the certification of deaths, the lack of specific information

on tumor characteristics, limited information at the individual level and the lack of cases to be able to perform an incidence analysis and show a more comprehensive analysis of what is happening in relation to breast cancer in each LAC country.

### **Conclusion**

This is the first study to analyze breast cancer mortality rates from 1997 to 2017 and create projections beyond 2030 in LAC countries. We discovered that breast cancer death rates rose in certain countries and fell in others during the study period. Similarly, the patterns of death from breast cancer varied dramatically across LAC countries based on age. Breast cancer mortality rates are expected to fall in Chile, Cuba, Paraguay, Peru, and Puerto Rico by 2030. To achieve the 2030 sustainable developmental goals, LAC countries should implement public health strategies to reduce mortality by breast cancer.

### **Declarations**

Ethics approval and consent to participate.

Not applicable

Consent for publication

Not applicable

Availability of data and materials

The datasets generated and/or analysed during the current study are available in the following link: <https://www.who.int/data/data-collection-tools/who-mortality-database>

Competing interests

The author(s) declare that they have no competing interests.

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Authors' contributions

Conceived and designed the idea: JSTR, JYM.

Had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis: JSTR, SL.

Contributed to the writing of the manuscript: All authors.

Contributed to the statistical analysis: JSTR, BV.

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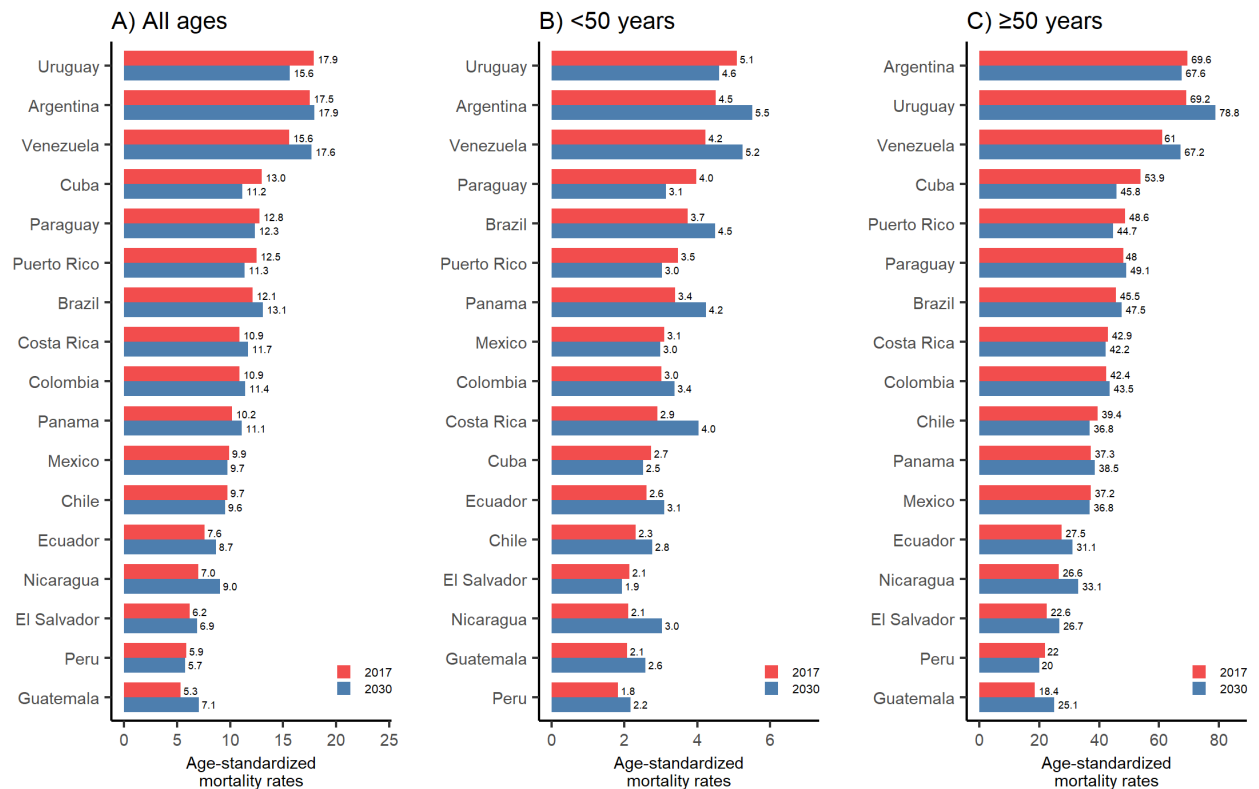
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**Figure Legends**

Figure 1. Age-standardized (SEGI's world standard population) breast cancer mortality rates per 100,000 in 2017\* and predicted for 2030\*\* in Latin America and the Caribbean.



\*Data from 2016 for Venezuela.

\*\*Age-standardized rate represents the mid-point for the projected period 2028-2032.

Figure 2. Breast cancer mortality trends (rates per 100,000 women-years, all ages, <50 years, and ≥50 years) 1997-2017 in Latin America and the Caribbean.

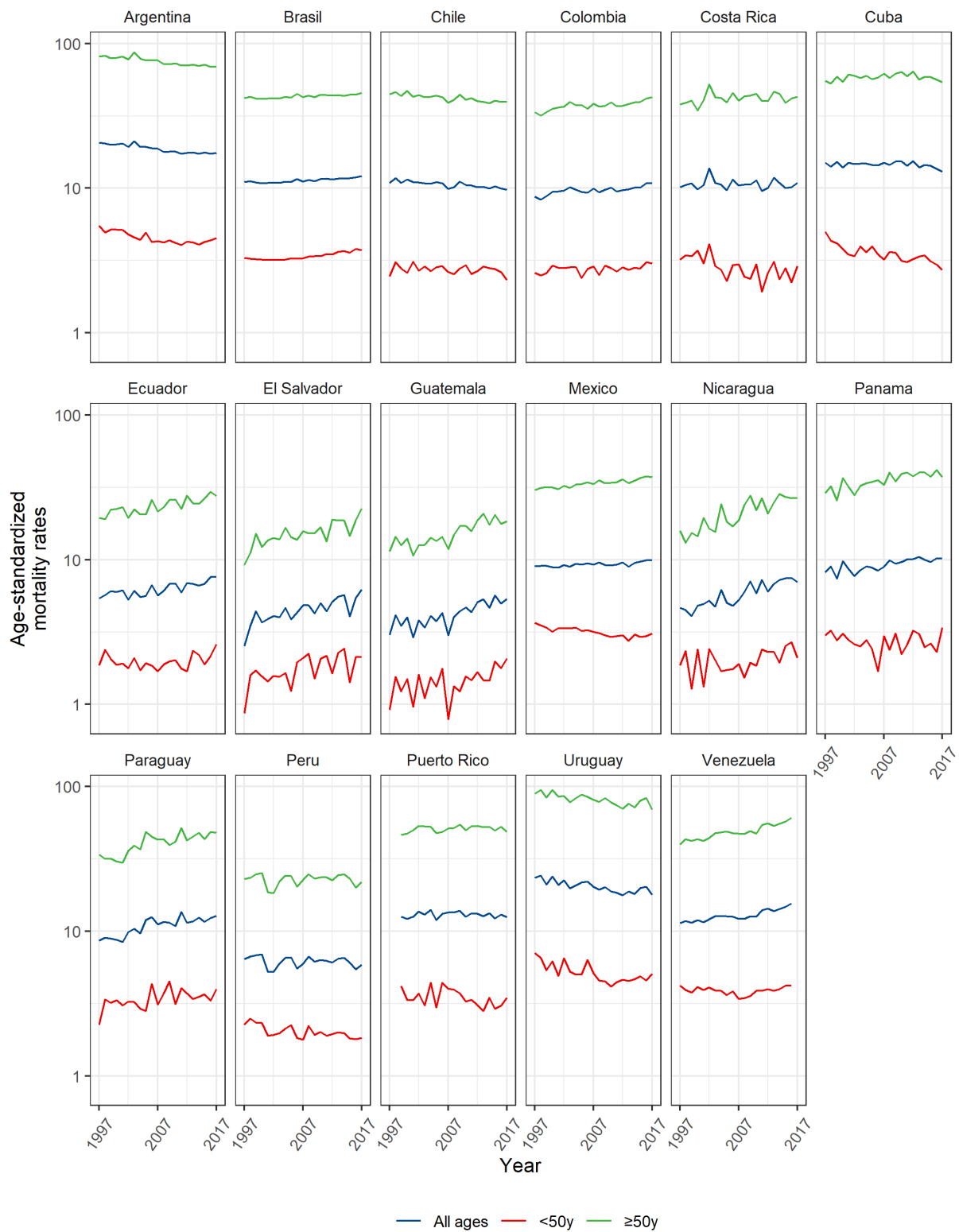


Figure 3. Average annual percent change (AAPC) and 95% confidence interval (CI) for breast cancer mortality rates in Latin America and the Caribbean, 1997-2017.

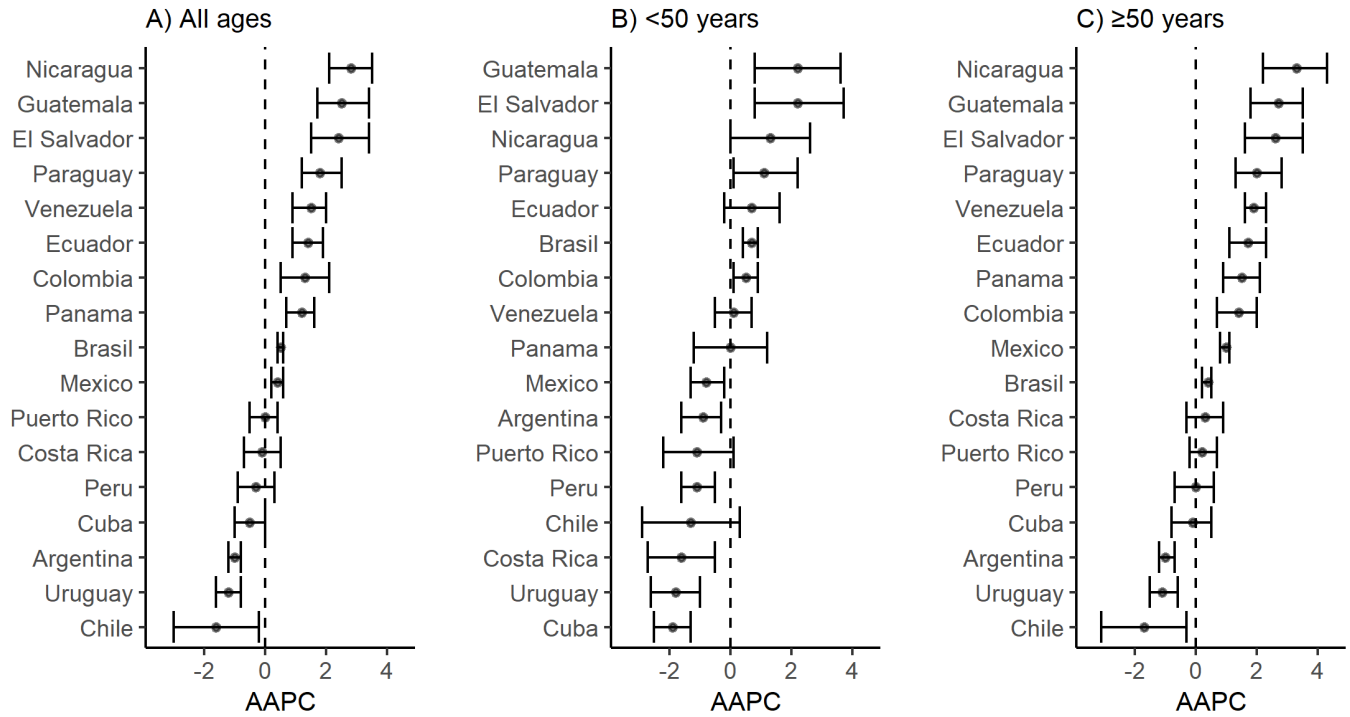




Table 1. Average annual percentage change (AAPC) with their 95% confidence intervals (95%CI) for age-adjusted breast cancer mortality rates among women of all ages in Latin America and the Caribbean, 1997-2017.

Countries	Calendar Years	EAPC	Period	APC	Period	APC	AAPC
<b>Argentina</b>	1997-2017	-1.0*(-1.2, -0.8)					-1.0*(-1.2, -0.8)
<b>Brasil</b>	1997-2017	0.5*(0.4, 0.6)					0.5*(0.4, 0.6)
<b>Chile</b>	1997-2017	-1.6*(-3.0, -0.2)					-1.6*(-3.0, -0.2)
<b>Colombia</b>	1997-2002	2.7*(0.2, 5.3)	2002-2013	0(-0.7, 0.7)	2013-2017	3.0*(0.5, 5.5)	1.3*(0.5, 2.1)
<b>Costa Rica</b>	1997-2017	-0.1(-0.7, 0.5)					-0.1(-0.7, 0.5)
<b>Cuba</b>	1997-2012	0.2(-0.2, 0.6)	2012-2017	-2.4*(-4.2, -0.6)			-0.5(-1.0, 0)
<b>Ecuador</b>	1997-2017	1.4*(0.9, 1.9)					1.4*(0.9, 1.9)
<b>El Salvador</b>	1997-2017	2.4*(1.5, 3.4)					2.4*(1.5, 3.4)
<b>Guatemala</b>	1997-2017	2.5*(1.7, 3.4)					2.5*(1.7, 3.4)
<b>Mexico</b>	1997-2017	0.4*(0.2, 0.6)					0.4*(0.2, 0.6)
<b>Nicaragua</b>	1997-2017	2.8*(2.1, 3.5)					2.8*(2.1, 3.5)
<b>Panamá</b>	1997-2017	1.2*(0.7, 1.6)					1.2*(0.7, 1.6)
<b>Paraguay</b>	1997-2017	1.8*(1.2, 2.5)					1.8*(1.2, 2.5)
<b>Peru</b>	1997-2017	-0.3(-0.9, 0.3)					-0.3(-0.9, 0.3)
<b>Puerto Rico</b>	1999-2017	0(-0.5, 0.4)					0(-0.5, 0.4)
<b>Uruguay</b>	1997-2017	-1.2*(-1.6, -0.8)					-1.2*(-1.6, -0.8)
<b>Venezuela</b>	1997-2009	0.8*(0.1, 1.4)	2009-2016	2.7*(1.6, 3.9)			1.5*(0.9, 2.0)

Table 2. Average annual percentage change (AAPC) with their 95% confidence intervals (95%CI) of for age-adjusted breast cancer mortality rates among women <50 years in Latin America and the Caribbean, 1997-2017.

<b>Countries</b>	<b>Calendar Years</b>	<b>APC (CI95%)</b>	<b>Calendar Years</b>	<b>APC (CI95%)</b>	<b>AAPC</b>
<b>Argentina</b>	1997-2017	-0.9*(-1.6, -0.3)			-0.9*(-1.6, -0.3)
<b>Brasil</b>	1997-2017	0.7*(0.4, 0.9)			0.7*(0.4, 0.9)
<b>Chile</b>	1997-2017	-1.3(-2.9, 0.3)			-1.3(-2.9, 0.3)
<b>Colombia</b>	1997-2017	0.5*(0.1, 0.9)			0.5*(0.1, 0.9)
<b>Costa Rica</b>	1997-2017	-1.6*(-2.7, -0.5)			-1.6*(-2.7, -0.5)
<b>Cuba</b>	1997-2017	-1.9*(-2.5, -1.3)			-1.9*(-2.5, -1.3)
<b>Ecuador</b>	1997-2017	0.7(-0.2,1.6)			0.7(-0.2,1.6)
<b>El Salvador</b>	1997-2017	2.2*(0.8, 3.7)			2.2*(0.8, 3.7)
<b>Guatemala</b>	1997-2017	2.2*(0.8, 3.6)			2.2*(0.8, 3.6)
<b>Mexico</b>	1997-2017	-0.8*(-1.3,-0.2)			-0.8*(-1.3,-0.2)
<b>Nicaragua</b>	1997-2017	1.3(-0.0,2.6)			1.3(-0.0,2.6)
<b>Panama</b>	1997-2017	-0.0(-1.2,1.2)			-0.0(-1.2,1.2)
<b>Paraguay</b>	1997-2017	1.1*(0.1, 2.2)			1.1*(0.1, 2.2)
<b>Peru</b>	1997-2017	-1.1*(-1.6, -0.5)			-1.1*(-1.6, -0.5)
<b>Puerto Rico</b>	1997-2017	-1.1(-2.2, 0.1)			-1.1(-2.2, 0.1)
<b>Uruguay</b>	1997-2017	-1.8*(-2.6, -1.0)			-1.8*(-2.6, -1.0)
<b>Venezuela</b>	1997-2008	-1.3*(-2.1, -0.5)	2008-2016	2.2*(1.0, 3.3)	0.1(-0.5, 0.7)

Table 3. Average annual percentage change (AAPC) with their 95% confidence intervals (95%CI) of for age-adjusted breast cancer mortality rates among women  $\geq 50$  years in Latin America and the Caribbean, 1997-2017.

Countries	Calendar Years	APC	Period	APC	Period	APC	AAPC
<b>Argentina</b>	1997-2017	-1.0*(-1.2, -0.7)					-1.0*(-1.2, -0.7)
<b>Brasil</b>	1997-2017	0.4*(0.2, 0.5)					0.4*(0.2, 0.5)
<b>Chile</b>	1997-2017	-1.7*(-3.1, -0.3)					-1.7*(-3.1, -0.3)
<b>Colombia</b>	1997-2003	2.7*(1.0, 4.4)	2003-2012	-0.2(-1.1, 0.7)	2012-2017	2.6*(1.1, 4.1)	1.4*(0.7, 2.0)
<b>Costa Rica</b>	1997-2017	0.3(-0.3, 0.9)					0.3(-0.3, 0.9)
<b>Cuba</b>	1997-2012	0.7*(0.2, 1.2)	2012-2017	-2.6*(-4.9, -0.2)			-0.1(-0.8, 0.5)
<b>Ecuador</b>	1997-2017	1.7*(1.1, 2.3)					1.7*(1.1, 2.3)
<b>El Salvador</b>	1997-2017	2.6*(1.6, 3.5)					2.6*(1.6, 3.5)
<b>Guatemala</b>	1997-2017	2.7*(1.8, 3.5)					2.7*(1.8, 3.5)
<b>México</b>	1997-2017	1.0*(0.8, 1.1)					1.0*(0.8, 1.1)
<b>Nicaragua</b>	1997-2017	3.3*(2.2, 4.3)					3.3*(2.2, 4.3)
<b>Panamá</b>	1997-2017	1.5*(0.9, 2.1)					1.5*(0.9, 2.1)
<b>Paraguay</b>	1997-2017	2.0*(1.3, 2.8)					2.0*(1.3, 2.8)
<b>Perú</b>	1997-2017	-0(-0.7, 0.6)					-0(-0.7, 0.6)
<b>Puerto Rico</b>	199-2017	0.2(-0.2, 0.7)					0.2(-0.2, 0.7)
<b>Uruguay</b>	1997-2017	-1.1*(-1.5, -0.6)					-1.1*(-1.5, -0.6)
<b>Venezuela</b>	1997-2016	1.9*(1.6, 2.3)					1.9*(1.6, 2.3)

Table 4. Number of breast cancer deaths, age-standardized mortality rates, and percentage change in cases due to population growth and risk among women in Latin America and the Caribbean, 2017 and predicted for 2030. (all ages)

Country	Female population (million per year)		Number of deaths in women of all ages		Age-standardized mortality rates		Total change, %	Change due to population, %	Change due to risk, %
	2017	2030	2017	2030	2017	2030			
Argentina	22.60	25.07	6024	7421	17.52	17.92	27.9	26.7	1.2
Brazil	107.44	114.24	16723	25368	12.10	13.09	65.1	50.6	14.5
Chile	9.28	9.85	1504	1904	9.73	9.56	30.1	37.7	-7.5
Colombia	24.93	27.22	3300	5151	10.89	11.41	75.1	58.9	16.3
Costa Rica	2.45	2.74	366	593	10.90	11.67	76.9	63.6	13.3
Cuba	5.67	5.62	1519	1699	12.96	11.17	12.0	30.8	-18.8
Ecuador	8.32	9.92	667	1144	7.60	8.70	97.7	59.2	38.5
El Salvador	3.25	3.62	217	220	6.22	6.89	87.1	40.9	46.2
Guatemala	8.68	10.74	352	739	5.35	7.08	129.9	66.8	63.0
México	65.44	71.96	6755	9746	9.93	9.74	58.2	52.8	5.5
Nicaragua	3.15	3.75	202	410	7.00	9.04	112.6	65.3	47.3
Panamá	2.02	2.47	241	508	10.18	11.09	129.4	107.0	22.4
Paraguay	3.36	3.92	391	556	12.78	12.32	56.8	53.8	3.0
Perú	16.10	18.16	1030	1517	5.86	5.74	52.4	58.4	-6.0
Puerto Rico	1.91	1.53	445	492	12.51	11.35	13.0	19.4	-6.4
Uruguay	1.79	1.84	204	260	17.91	15.60	7.0	23.4	-16.4
Venezuela*	16.54	17.06	2513	1289	15.58	17.65	77.5	47.6	29.9

Supplementary 1. Number of breast cancer deaths, age-standardized mortality rates, and percentage change in cases due to population growth and risk among women in Latin America and the Caribbean, 2015 and predicted for 2030. (<50 years)

Country	Female population (million per year)		Number of deaths in women of all ages		Age-standardized mortality rates		Total change, %	Change due to population, %	Change due to risk, %
	2017	2030	2017	2030	2017	2030			
Argentina	16.43	17.40	838	1183	4.51	5.51	55.0	20.2	34.8
Brazil	80.31	76.14	3761	5026	3.74	4.49	39.2	14.3	24.9
Chile	6.38	6.18	197	249	2.31	2.76	10.1	7.0	3.1
Colombia	18.94	18.64	689	856	3.01	3.38	31.7	12.6	19.1
Costa Rica	1.81	1.83	63	109	2.90	4.04	89.3	24.5	64.8
Cuba	3.53	3.07	163	117	2.73	2.52	-39.3	-24.7	-14.6
Ecuador	6.65	7.41	178	267	2.61	3.10	82.3	30.8	51.5
El Salvador	2.55	2.64	57	62	2.13	1.93	14.4	21.8	-7.4
Guatemala	7.48	8.81	121	233	2.08	2.58	131.9	58.4	73.5
Mexico	52.38	52.10	1796	1942	3.09	2.98	17.9	16.8	1.1
Nicaragua	2.61	2.87	54	106	2.10	3.03	87.3	42.2	45.0
Panama	1.58	1.78	60	148	3.40	4.24	210.7	102.2	108.5
Paraguay	2.77	3.11	93	109	3.98	3.14	33.6	53.4	-19.8
Peru	12.77	13.10	250	361	1.83	2.17	45.4	24.5	20.9
Puerto Rico	1.24	771	59	35	3.48	3.03	-35.6	-32.7	-2.9
Uruguay	1.19	1.15	75	69	5.10	4.60	0.6	4.3	-3.7
Venezuela	13.55	12.49	548	798	4.23	5.25	50.3	17.9	32.4

Supplementary 2. Number of breast cancer deaths, age-standardized mortality rates, and percentage change in cases due to population growth and risk among women in Latin America and the Caribbean, 2015 and predicted for 2030.( ≥50 years)

Country	Female population (million per year)		Number of deaths in women of all ages		Age-standardized mortality rates		Total change, %	Change due to population, %	Change due to risk, %
	2017	2030	2017	2030	2017	2030			
Argentina	6.17	7.67	5186	6237	69.56	67.57	23.7	27.6	-3.9
Brazil	27.13	38.10	12962	20341	45.53	47.49	73.1	61.8	11.3
Chile	2.90	3.66	1307	1654	39.44	36.77	33.8	43.3	-9.5
Colombia	5.99	8.58	2611	4295	42.40	43.51	87.5	72.0	15.4
Costa Rica	0.64	915	303	484	42.91	42.16	74.3	71.7	2.7
Cuba	2.14	2.55	1356	1581	53.90	45.79	-39.3	-24.7	-14.6
Ecuador	1.67	2.51	489	876	27.52	31.06	103.0	68.8	34.1
El Salvador	0.69	981	160	289	22.60	26.69	116.8	48.7	68.1
Guatemala	1.21	1.92	231	506	18.42	25.08	128.9	70.7	58.2
Mexico	13.06	19.87	4959	7803	37.25	36.80	73.7	66.0	7.7
Nicaragua	0.55	875	148	304	26.57	33.10	123.1	74.8	48.3
Panama	0.45	686	181	359	37.31	38.47	107.0	108.3	-1.4
Paraguay	0.59	818	298	446	48.00	49.10	30.7	57.9	-27.2
Peru	3.33	5.07	780	1156	21.95	20.05	54.7	69.7	-15.0
Puerto Rico	0.67	754	386	458	48.64	44.66	19.8	26.7	-6.9
Uruguay	0.60	684	536	699	69.16	78.76	22.7	17.4	5.3
Venezuela	2.99	4.58	2186	3322	61.01	67.20	85.6	56.4	29.2

## Introduction

In 2020, breast cancer was one of the most frequently diagnosed and deadliest malignancies in women worldwide, with more than 2 million new cases (24.5% of all cancers) and more than 600,000 deaths (15.5% of all cancers) (1), mainly affecting middle- and low-income countries (2).

Breast cancer is also the most frequent neoplasm among women in Latin America and the Caribbean (LAC) (except in Bolivia, Paraguay, and Peru) (1), with an increase in both the incidence and mortality rates (1, 3). Since the 1990s, there has been a steady increase in breast cancer mortality rates worldwide, with the highest rates being found in LAC (4). However, the increase in incidence and mortality in LAC has been heterogeneous in the different countries. For example, between 1992 and 2012, Brazil showed an increase in breast cancer mortality, mainly in the age group of 50 to 69 years (5). While in Colombia, in 2018, breast cancer was the leading cause of death from cancer (mortality rate of 10.48 per 100,000 persons) (6). Finally, from 2003 to 2017, the average mortality rate in Peru was 9.97 per 100,000 women (7).

These geographic variations in breast cancer mortality may be due to socioeconomic status, lifestyles, and access to timely care in each country (8-11). Premenopausal women were found to have a higher risk of breast cancer than age-matched postmenopausal women (12-14).

Previous studies in the LAC population have been limited to short periods of time and a limited number of countries, not allowing exhaustive comparison of the evolution of breast cancer trends in this region. In addition, it is important to know how mortality rates have evolved in the last two decades and what patterns will follow in the coming years, with the goal of proposing containment measures for each country in order to reduce mortality by this neoplasm. Therefore, our objective was to provide breast cancer mortality rates between 1997 and 2017 for LAC countries and predict their mortality rates for the year 2030.

## **Materials and Methods**

### **Data source**

We conducted an observational study with an ecological design. The World Health Organization (WHO) mortality database was used, which compiles death registration data from member states and includes information on causes of death. This mortality database is freely accessible at the following link: <https://www.who.int/data/data-collection-tools/who-mortality-database>.

Mortality data for LAC countries were extracted for the period from 1997 (or first available year) to 2017 (or latest available year). Breast cancer deaths were identified with the code C50 (ICD-10: malignant neoplasm of the breast). The analysis was performed for 5-year age intervals (0-4, 5-9, 10-14, ..., 85 and over). Projected population estimates for the study countries were obtained from World Population Prospects (15).

### **Age adjusted mortality rates**

We estimated age-standardized mortality rates per 100,000 female-years by the direct method using the SEGI world standard population (16). The analysis was performed for 5-year age intervals (0-4, 5-9, 10-14, ..., 85 and older), also divided into two groups, <50 years and  $\geq 50$  years. Age-specific mortality trends were estimated using Poisson models with the Joinpoint regression program version 4.7.0. Joinpoints given by the program were identified and the annual percentage change (APC) and corresponding 95% confidence intervals (95%CI) were estimated for each country. The APC were considered statistically significant with a p-value <0.05.



### Predictions of mortality rates

Predictions for the year 2030 were made using the Nordpred package in the R software, based on an age-period-cohort model. An evaluation was made between the last observed period and the last projected period. The predicted data were compared with the expected rate if the rate found for the observed period was maintained in the projected period in each of the age groups evaluated. This evaluation made it possible to identify whether the difference was due to changes in the structure and size of the population or to an increased risk of death from breast cancer, as proposed by Møller et al. using the formula (17):

$$\Delta_{tot} = \Delta_{risk} + \Delta_{pop} = (N_{ff} - N_{off}) + (N_{off} - N_{ooo})$$

Where:

$\Delta_{tot}$ : The total change between the two periods analyzed.

$\Delta_{risk}$ : The change as a function of risk.

$\Delta_{pop}$ : Is the change as a function of changes in population size and structure.

$N_{ooo}$ : The number of observed cases.

$N_{ff}$ : The number of predicted cases.

$N_{off}$ : is the number of expected cases using the rate of the observed period to the population of the last predicted period.

This study was approved by the Institutional Research Ethics Committee of the Universidad Científica del Sur (CIEI-CIENTÍFICA) (449-2021-POS50).

## Results

Figure 1 shows breast cancer mortality rates for the latest available year and their prediction for the year 2030 in LAC countries. In 2017, Argentina (17.5), Venezuela (16.4), and Uruguay (15.2) had the highest mortality rates for all ages, whereas in 2030 Argentina (17.9), Uruguay (15.6), and Brazil (13.1) will have the highest mortality rates.

Table 1 presents the estimated annual percentage change for age-adjusted mortality rates of breast cancer in LAC countries. Brazil (+0.5%), Ecuador (+1.4%), El Salvador (+2.2%), Guatemala (+2.5%), Mexico (+0.4%), Nicaragua (+2.8%), Panama (+1.2%), and Paraguay (+1.8%) reported upward trends between 1997 to 2017, while Argentina (-1.0%), Chile (-1.6%), and Uruguay (-1.2%) had downward trends (Figure 2, and Figure 3).

In women under 50 years of age, the mortality rates by breast cancer in Argentina (-0.9%), Costa Rica (-1.6%), Cuba (-1.9%), Mexico (-0.8%), Peru (-1.1%) and Uruguay (-1.8%) significantly decreased, while Brazil (+0.7%), Colombia (+0.5%), El Salvador (+2.4%), Guatemala (+2.2%), and Paraguay (+1.1%) showed significant increases during the study period (Table 2, Figure 2, and Figure 3).

In women aged 50 years and older, mortality rates by breast cancer significantly decreased in Argentina, Chile, and Uruguay during the study period, while in Brazil, Ecuador, El Salvador, Guatemala, Mexico, Nicaragua, Panama, Paraguay, and Venezuela these values significantly increased. (Table 3, Figure 2, and Figure 3). Colombia had a significant increase in deaths (+2.7%) between 1997 and 2003, subsequently maintained stable trends between 2003 and 2012, and then presented an increase of 2.6% in the last period (2012-2017). While Cuba had an increase of 0.7% between 1997 and 2012, which then decreased (-2.6%) until 2017.

According to the predictions for 2030, in women of all ages, most countries showed increases in mortality rates between 2017 and 2030. In some countries, such as Chile, Cuba, Mexico,

Paraguay, Peru, Puerto Rico, and Venezuela, the mortality rates will decrease. In terms of structural changes according to deaths and population, population structure will increase in all countries, whereas in Chile (-7.5%), Cuba (-18.8%), El Salvador (-6.2%), Panamá (-23.6%), Perú (-6%), Puerto Rico (-6.4%), Uruguay (-16.4%) and Venezuela (-44%) the risk of death from this disease will decrease (Table 4).

In women <50 years, the population structure in Cuba and Puerto Rico will decrease by the year 2030, which will positively influence the total change in mortality by breast cancer. Panama will have the greatest increase in population change and change due to risk, which will negatively influence this disease (Supplementary 1). On the other hand, in women  $\geq 50$  years, Cuba will show a decrease in breast cancer mortality, mainly due to a change in its population structure (Supplementary 2).

## Discussion

In this study, mortality trends for breast cancer between 1997 and 2017 were compared across LAC countries, and mortality for 2030 was predicted. Certain LAC countries recorded increases in breast cancer death rates of more than 2% annually, while others reported decreases of 1% to 1.6%. Between 1997 and 2027, mortality patterns from breast cancer varied significantly throughout LAC countries depending on the age cutoff of women older and younger than 50 years. The breast cancer mortality rates in Chile, Cuba, Mexico, Paraguay, Peru, Puerto Rico, and Venezuela are expected to decrease by 2030, although these changes will not be significant. We found that between 1997 and 2017 Argentina, Uruguay, and Venezuela had the highest breast cancer mortality rates in the region. These results reflect current trends reported by GLOBOCAN for the year 2020, which indicate that these three countries had the highest rates in the region (more than 17 deaths per 100,000) (1). These rates are only comparable to African countries which report rates above 20 deaths per 100,000. One of the main risk factors for the

development of breast cancer is age, with changes in demographic structure leading to epidemiological changes in which breast cancer will reach epidemic proportions in LAC. In addition, differences in mortality between countries could be explained by variations in prevention strategies, access to health services, health insurance coverage and patient care practices (i.e., the lack of specialists in the rural areas of each country or specialized institutes for comprehensive cancer management). The inequalities in access to breast cancer care are strikingly visible within the region, and this is evidenced by the mortality outcomes in many of the countries reported in this study.

The disparity in mortality rates between LAC countries for women over and under 50 years old remains significant. When compared to older women, younger women have worse prognoses and a higher risk of breast cancer recurrence and mortality (18, 19). Several studies (20-22) have investigated risk variables that may affect the incidence of breast cancer in different countries. Demographic, socioeconomic, genetic, and lifestyle-related risk variables, as well as reproductive behavior, are the most important risk factors. Age is still the most important factor in the occurrence of breast cancer. Brazil, Colombia, El Salvador, Guatemala, and Paraguay showed significant increases in breast cancer mortality in women under and over 50 years old between 1997 and 2017. As most Latin American countries migrate to a more advanced population age structure, demographic shifts in the region are causing an epidemiological transition. Currently, 6.9% of the Brazilian population is 65 years of age or older. By 2030, the number of women aged 60 and up will have doubled, dramatically increasing the number of breast cancer cases. The inclusion of mammography screening in primary care programs, as well as the adoption of quality standards, are likely to have played a role in improving diagnoses in these nations. Women are diagnosed earlier in Brazil, particularly in affluent regions, albeit at a far lower rate than in Sweden. Several LAC studies have found an adverse relationship

between the diagnosis of late-stage breast cancer and survival (23-25). According to studies conducted in Brazil (26) and Colombia (27), the annual costs of treating patients with stage IV breast cancer are three- to four-times higher than those of patients with stage I breast cancer because the stage of diagnosis affects outcomes and, thus, the burden of disease in societies. More investment in health systems in LAC countries is required for early detection of breast cancer, earlier diagnosis, and accessible and inexpensive treatment for all women.

Some LAC countries are expected to see reductions in breast cancer mortality rates by 2030. Argentina, Brazil, Paraguay, Uruguay, and Venezuela will have the highest mortality rates in the area, with more than 12 deaths per 100,000 people, while El Salvador and Peru will have the lowest, with less than 6 fatalities per 100,000 people. Our estimations exceed those reported in Los Angeles and Western European countries (28). The limited availability of screening and the time lag between initial suspicion of breast cancer and diagnosis are two characteristics that can affect clinical results, and that inferior access to treatment also has an impact on clinical outcomes (29, 30). Latin American women are diagnosed at a younger age than women in North America and Europe (31). Early menarche, late-term pregnancy, nulliparity, and a lack of nursing are well-known risk factors for breast cancer occurrence (32). Furthermore, lifestyle behaviors such as nutrition and obesity, as well as environmental variables, may contribute to adverse trends in young women (32). To improve future outcomes, programs must be structured and new interventions welcomed.

This study presents the usual limitations of a cancer registry analysis of a secondary database, such as the quality and validity of the certification of deaths, the lack of specific information on tumor characteristics, limited information at the individual level and the lack of cases to be able to perform an incidence analysis and show a more comprehensive analysis of what is happening in relation to breast cancer in each LAC country.

## **Conclusion**

This is the first study to analyze breast cancer mortality rates from 1997 to 2017 and create projections beyond 2030 in LAC countries. We discovered that breast cancer death rates rose in certain countries and fell in others during the study period. Similarly, the patterns of death from breast cancer varied dramatically across LAC countries based on age. Breast cancer mortality rates are expected to fall in Chile, Cuba, Mexico, Paraguay, Peru, Puerto Rico, and Venezuela by 2030. To achieve the 2030 sustainable developmental goals, LAC countries should implement public health strategies to reduce mortality by breast cancer.

## **Declarations**

Ethics approval and consent to participate

Not applicable

Consent for publication

Not applicable

Availability of data and materials

The datasets generated and/or analysed during the current study are available in the following link: <https://www.who.int/data/data-collection-tools/who-mortality-database>

Competing interests

The author(s) declare that they have no competing interests.

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Authors' contributions

Conceived and designed the idea: JSRT, JYM

Had full access to all the data in the study and take responsibility for the integrity of the data

and the accuracy of the data analysis: JSRT, SL

Contributed to the writing of the manuscript: All authors.

Contributed to the statistical analysis: JSTR, BV

Critical revision of the manuscript: CSA, YHR

Approval of the submitted and final version: All authors.

Acknowledgments

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June 26, 2023

Dra. Natalie Pafitis,  
Senior Editor  
BMC Public Health

Reference: 45cf7114-422b-47fe-8780-669639e5609a | v.1.1

Dear Dra Natalie Pafitis,

We greatly appreciate the consideration given to our manuscript and the valuable comments made by the reviewers. Below we present a point-by-point response to the comments. As requested, we have highlighted the changes that were made from the previous version in the attached revised document.

We are grateful for the opportunity to publish our research work in your new journal. All co-authors have seen and agree with this resubmission.

Thank you for your consideration of our manuscript.

Sincerely,



J. Smith Torres Román, MD  
Universidad Científica del Sur, Lima, Perú  
Tel: +(51) 99 321-9508  
Email: [jstorresroman@gmail.com](mailto:jstorresroman@gmail.com)

**Reviewer #1:**

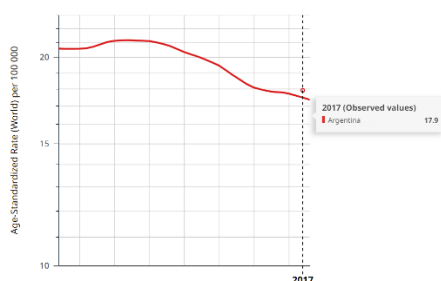
**This is a very interesting paper indeed. Breast cancer (BC) mortality is, because of its magnitude a very relevant topic, especially for the Latin America and Caribbean (LAC) region. It's really remarkable the effort that the authors had made, to perform such a detailed analysis of mortality data by country and age groups. Although is true that information is rather scarce in the LAC region, some authors had already published trends analysis before. Those precedent research are likely not as detailed nor they include as much countries as the present. Still, I believe that some of those pioneer papers, (\*) should be considered to be included in the references, as they could provide interesting input for comparison purposes.**

**Just few questions:**

- 1) On the other hand, I have some issues, regarding projected Age Standardized Mortality Rates (ASMR) for 2030. Compared to time trends, from 1997 to 2017; projections results are puzzling. It's quite easy to understand that, if a given increase is projected for a population, an increase in the number of cases (or deaths) shall be expected. This is usually presented under the assumption of stable rates. However, it seems quite odd that the ASMR are projected to decline for 2030 for most countries that had displayed monotonous increase (up to 2% APC) along the 20 previous years, Conversely, for countries such as Argentina and Uruguay, which had presented until 2017 decreasing trends, (APC over 1%) confirmed for both segments (up to 50 and 50+ years), ASMR are projected to slightly increase for 2030. I think those results deserve a thorough revision of the applied model. If results were confirmed, some explanation must be provided to help readers to understand those forecasted shifts in mortality trends or predictions might be excluded and saved for some other article in the future.

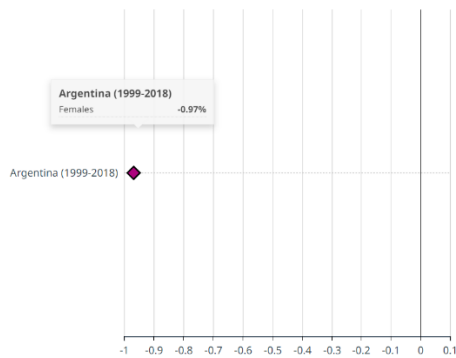
Authors: Thank you very much for your comment. We have again revised the predictions. We have again reviewed countries such as Argentina, which is correct that the APC decreases significantly. However, we have compared results with those published with GLOBOCAN and see that they are similar (identical) in many analyses. This may be due to changes in the population, because if we look at the change in risk it is only 1.2%, however the total change is mainly due to the change in population that this country will have for women.

Age-standardized rate (World) per 100 000, mortality, females  
Breast  
Argentina



**Estimated annual percentage change of ASR (World) per 100 000, mortality, females**

Breast  
Argentina

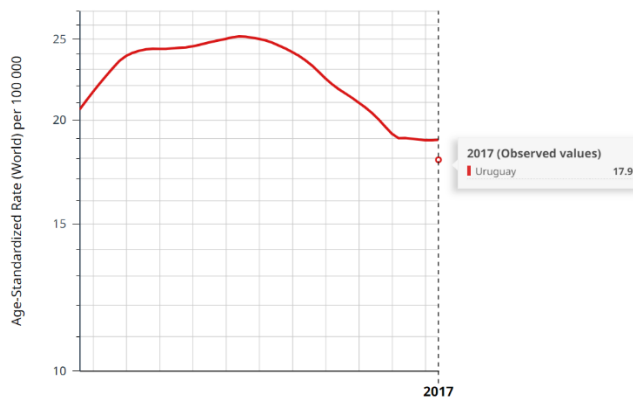


Estimated Annual Percentage Change (%)

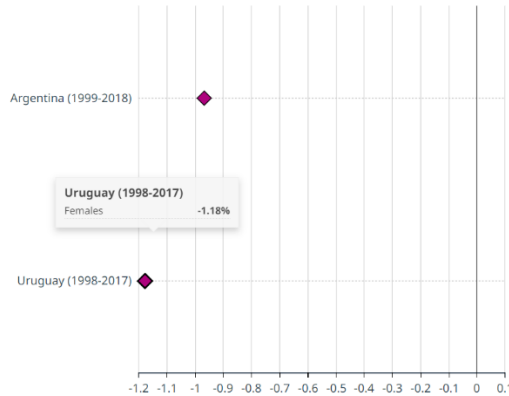
Cancer id	Cancer label	Population id	Population	Sex	Type	Cases base in 2020	Year	Prediction	Risk change	Risk percentage (%)
20	Breast	32	Argentina	2	1	6821	2020	6821	0	0
20	Breast	32	Argentina	2	1	6821	2025	7432	648	9.5
20	Breast	32	Argentina	2	1	6821	2030	8109	1370	20.1
20	Breast	32	Argentina	2	1	6821	2035	8826	2138	31.3
20	Breast	32	Argentina	2	1	6821	2040	9553	2925	42.9

**Age-standardized rate (World) per 100 000, mortality, females**

Breast  
Uruguay



Estimated annual percentage change of ASR (World) per 100 000, mortality, females  
Breast  
Uruguay

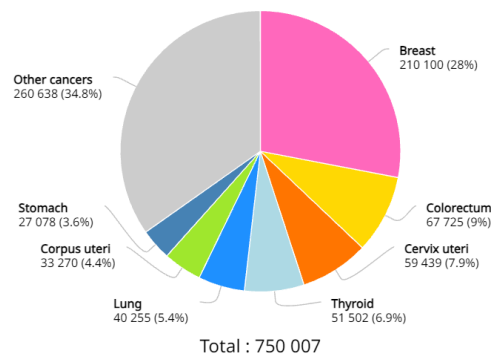


We have checked the other countries and we see that everything is correct.

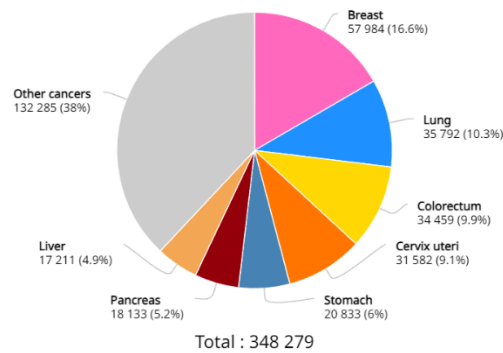
- 2) In the Introduction It is not clear if the statement “BC is the most frequent neoplasm among women in LAC except in Bolivia, Paraguay, and Peru” refers to incidence or mortality. Anyway, it is not accurate for either (incidence, nor mortality), according to the cited source gco.iarc.fr. Please check.

Authors: Thank you very much for your comment. We have corrected some lines, however, breast cancer is the most frequent and the one with the highest mortality among women in the region. Attached are some images from GLOBOCAN.

Estimated number of new cases in 2020, Latin America and the Caribbean, females, all ages



Estimated number of deaths in 2020, Latin America and the Caribbean, females, all ages



Source: GLOBOCAN 2020.

Reference: An updated profile of the cancer burden, patterns and trends in Latin America and the Caribbean (Marion Pineros et al. The Lancet 2022)

- 3) In Methods, as SEGI corresponds to the last name of the Japanese scientist that described the World Standard Population (Prof. Mitsuo Segi), I don't think it is correct to use capital letters, as if it were an acronym.

Authors: Thank you very much for your comment. We agree with the reviewer.

- 4) I didn't find an explanation for part A, B and C in figure 1. (My guess, "all ages" "below 50" and "50 plus"?)

Authors: The assumption is correct. We have placed it.

- 5) I did quite not understand the point of comparing those countries with the highest ASMR in South America with African countries, as this comparison, if incidence and M/I rate ratio is not considered is confusing and misleading. The comparison might be valid for some anglophone Caribbean countries, not included for this article, such as Barbados, Jamaica and Bahamas.

Authors: Thank you very much for your comment. We agree with the reviewer.

**Reviewer #2:**

**The objective of this study was to determine the breast cancer mortality rates between 1997 and 2017 for LAC countries and predict mortality until 2030. I consider it is a very important issue in public health, and it is necessary to analyze it in Latin-American countries.**

- 1) The title is correct and clear. The introduction is adequate. Methodology is well developed and it is adequate to respond to the study objective. More explanation about

quality of databases is necessary, because mortality databases in Latin-American countries sometimes have omission problems. Indeed, sometimes there are problems with the high percentage of omission of age, sex or death codification. How the authors affront this problem?

Authors: Thank you very much for your comment. We are well aware of the registration problems in Latin American countries. For this reason, we have added several points in the limitations section.

2) Results: Figure 1 and 3, the authors must clear what is the meaning of A, B and C.

Authors: Thank you very much for your comment. We have added the meanings.

3) Discussion: More discussion is necessary about socioeconomic and lifestyle factors in the analyzed countries and their possible influences in the observed results.

Authors:

Thanks for your comments. We include more discussion about socioeconomic factors and lifestyles; this significantly improves our presentation and approach. [Page 6 and 7]

## **Resumen**

### **Antecedentes**

El cáncer de mama es una de las principales causas de mortalidad por cáncer entre las mujeres de América Latina y el Caribe (ALC), pero se carece de un análisis exhaustivo y actualizado de las tendencias de mortalidad. El objetivo de este estudio fue determinar la evolución de las tasas de mortalidad por cáncer de mama entre 1997 y 2017 para los países de ALC y predecir la mortalidad hasta 2030.

### **Métodos**

Se recolectaron las muertes por cáncer de mama en 17 países de ALC de la base de datos de mortalidad de la Organización Mundial de la Salud. Se estimaron las tasas de mortalidad estandarizadas por edad por 100,000 mujeres-año. Las tendencias de mortalidad se evaluaron con análisis de regresión Joinpoint por país y grupos de edad (todas las edades, <40 años, 40-59 años y  $\geq 60$  años). Para 2030, predecimos el número de muertes, las tasas de mortalidad, los cambios en la estructura y el tamaño de la población y el riesgo de muerte por cáncer de mama.

### **Resultados**

Argentina, Uruguay y Venezuela registraron las tasas de mortalidad más elevadas durante todo el periodo de estudio. Guatemala, El Salvador y Nicaragua registraron los mayores aumentos (de 2,4% a 2,8% anual), mientras que Argentina, Chile y Uruguay registraron tendencias a la baja (de -1,0 a -1,6% anual). En mujeres <40y, tres países presentaron tendencias a la baja y cuatro países mostraron tendencias al alza, mientras que en mujeres  $\geq 60$  años, tres países presentaron tendencias decrecientes y once mostraron tendencias crecientes. En 2030, se esperan aumentos en la región de ALC, principalmente en Guatemala (+63,0%), Nicaragua (+47,3), El Salvador (+46,2%), Ecuador (+38,5%) y Venezuela (+29,9%).

### **Conclusión**

Nuestros hallazgos sugieren diferencias considerables en la mortalidad por cáncer de mama en los países de ALC por grupos de edad. Para alcanzar los objetivos de desarrollo sostenible de 2030, los países de ALC deben implementar estrategias de salud pública para reducir la mortalidad por cáncer de mama.



## Abstract

### Background

Breast cancer is among the leading cause of cancer-related mortality among Latin American and Caribbean (LAC) women, but a comprehensive and updated analysis of mortality trends is lacking. The objective of this study was to determine the evolution of breast cancer mortality rates between 1997 and 2017 for LAC countries and predict mortality until 2030.

### Methods

We retrieved breast cancer deaths across 17 LAC countries from the World Health Organization mortality database. Age-standardized mortality rates per 100,000 women-years were estimated. Mortality trends were evaluated with Joinpoint regression analyses by country and age group (all ages, <40 years, 40-59 years, and  $\geq 60$  years). By 2030, we predict number of deaths, mortality rates, changes in population structure and size, and risk of death from breast cancer.

### Results

Argentina, Uruguay, and Venezuela reported the highest mortality rates throughout the study period. Guatemala, El Salvador, and Nicaragua reported the largest increases (from 2.4% to 2.8% annually), whereas Argentina, Chile, and Uruguay reported downward trends (from  $-1.0$  to  $-1.6\%$  annually). In women <40y, three countries presented downward trends and four countries showed increasing trends, where in women  $\geq 60$ y, three countries had decreased trends and twelve showed increased trends. In 2030, increases are expected in the LAC region, mainly in Guatemala (+63.0%), Nicaragua (+47.3), El Salvador (+46.2%), Ecuador (+38.5%) and Venezuela (+29.9%).

### Conclusion

Our findings suggest considerable differences in breast cancer mortality across LAC countries by age group. To achieve the 2030 sustainable developmental goals, LAC countries should implement public health strategies to reduce mortality by breast cancer.

## Introducción

En 2020, el cáncer de mama fue la neoplasia maligna más diagnosticada y con la mayor mortalidad en las mujeres a nivel mundial, con más de 2 millones de casos nuevos (24,5% de todos los cánceres) y más de 600,000 muertes (15,5% de todos los cánceres) [1], afectando principalmente a países de medianos y bajos ingresos [2].

En América Latina y el Caribe (ALC), el cáncer de mama es también la neoplasia más frecuente entre las mujeres [1, 3] En las últimas décadas, se ha producido un aumento significativo de las tasas de mortalidad por cáncer de mama en la mayoría de los países a nivel mundial, encontrándose el aumento más significativo en la región de ALC [4]. Sin embargo, hasta la fecha no existen estudios que permitan realizar una comparación exhaustiva de la evolución de las tendencias de mortalidad por cáncer de mama en esta región. Además, que tampoco se ha realizado una comparación entre diferentes grupos etarios para conocer el impacto que tiene esta neoplasia en ALC.

Las variaciones en la mortalidad por cáncer de mama pueden deberse al nivel socioeconómico, estilos de vida y acceso a una atención oportuna en cada país [5-8]. Debido a esto, en el 2021, se implementó la Iniciativa Mundial contra el cáncer de mama de la OMS, el cual tiene como objetivo reducir las desigualdades y reducir la mortalidad por cáncer de mama [9]. Por tal motivo, es importante conocer cómo ha evolucionado la mortalidad por cáncer de mama en nuestra región. Además, resulta de suma importancia conocer que cifras podríamos esperar para los próximos años en caso de continuar con estas mismas tendencias, con el fin de proponer medidas de contención para cada país.

Como mencionamos, los estudios previos en la población de ALC se han limitado a periodos cortos de tiempo y a un número limitado de países, lo que no permite una comparación exhaustiva de la evolución de las tendencias del cáncer de mama en esta región. Por lo tanto,

nuestro objetivo fue estimar las tasas de mortalidad por cáncer de mama entre 1997 y 2017 para los países de ALC y predecir sus tasas de mortalidad para el año 2030.

## **Materiales y métodos**

### **Origen de los datos**

Se realizó un estudio observacional con un diseño ecológico de series temporales. Se utilizó la base de datos de mortalidad de la Organización Mundial de la Salud (OMS). Esta base de datos se construye de las defunciones registradas en los sistemas nacionales de registro civil, con la causa de defunción subyacente codificada por la autoridad nacional competente. Estos datos son estadísticas nacionales oficiales transmitidos a la OMS por las autoridades competentes de los países incluidos. Cada Estado miembro comunica los datos de población junto con sus datos de mortalidad, para la población cubierta por el sistema de registro de defunciones, de conformidad con las normas de la Clasificación Internacional de Enfermedades (CIE) 10a. revisión. Sólo se han incluido datos de los países que comunican datos debidamente codificados según la CIE.

Esta base de datos de mortalidad es de libre acceso en el siguiente enlace:

<https://www.who.int/data/data-collection-tools/who-mortality-database>

Se extrajeron los datos de mortalidad de los países de ALC para el periodo comprendido entre 1997 (o primer año disponible) y 2017 (o último año disponible). Las muertes por cáncer de mama se identificaron con el código C50 (CIE-10a. revisión: neoplasia maligna de mama). El análisis se realizó para intervalos de edad de 5 años (0-4, 5-9, 10-14, ..., 85 y más). Las estimaciones de población previstas para los países del estudio se obtuvieron de World Population Prospects [10].

### **Tasas de mortalidad ajustadas por edad**

Estimamos las tasas de mortalidad estandarizadas por edad por 100,000 mujeres-año mediante el método directo utilizando la población estándar mundial WHO World Standard . Además, realizamos un análisis secundario utilizando la población SEGI [11], con la finalidad de comparar las tasas de mortalidad y la evolución de estas durante los años de estudio. El análisis se realizó para intervalos de edad de 5 años (0-4, 5-9, 10-14, ..., 85+), también fueron divididos en los siguientes grupos etarios: <40 años, 40-59 años, y  $\geq 60$  años. Las tendencias de mortalidad específicas por edad se estimaron utilizando modelos de Poisson con el programa de regresión Joinpoint versión 4.7.0. Se identificaron los puntos de unión dados por el programa y se estimó el cambio porcentual anual (CPA) y los correspondientes intervalos de confianza del 95% (IC95%) para cada país. Los CPA se consideraron estadísticamente significativos con un valor  $p < 0,05$ . Calculamos CPA promedio (CPAM) para los países que tenían 2 o más puntos de unión. Para caracterizar las tendencias, seguimos la metodología utilizada por el Instituto Nacional del Cáncer (Departamento de Salud y Servicios Humanos de EE.UU.). Si la tendencia no era estadísticamente significativa, se consideraba "estable" cuando  $-0,5 \leq APC \leq 0,5$  o se definía como "cambio no significativo" cuando  $APC < -0,5$  o  $APC > 0,5$ . Pero si había significación estadística, la tendencia se caracterizaba como "ascendente" cuando  $APC > 0$  o como "descendente" cuando  $APC < 0$ .

### **Predicciones de las tasas de mortalidad**

Las predicciones para el año 2030 se realizaron utilizando el paquete Nordpred del programa informático R, basado en un modelo edad-periodo-cohorte. Se realizó una extrapolación de las tendencias basada en las tasas observadas cada 5 años (es decir, 2003-2007, 2008-2012 y 2013-2017) para los tres periodos próximos (es decir, 2018-2022, 2023-2027 y 2028-2032). Para el periodo previsto, se utilizó la mediana de la población del año que representaba la mitad de los

periodos quinquenales (es decir, 2020, 2025 y 2030). Se utilizó el método de la tendencia cortada para atenuar la deriva lineal en un 0%, 25% y 50%, del primero al tercer periodo, respectivamente.

Se realizó una evaluación entre el último periodo observado y el último periodo previsto. Los datos previstos se compararon con la tasa esperada si la tasa encontrada para el periodo observado se mantenía en el periodo proyectado en cada uno de los grupos de edad evaluados. Esta evaluación permitió identificar si la diferencia se debía a cambios en la estructura y el tamaño de la población o a un mayor riesgo de muerte por cáncer de mama, como proponen Møller et al. mediante la fórmula [12]:

$$\Delta_{tot} = \Delta_{risk} + \Delta_{pop} = (N_{fff} - N_{off}) + (N_{off} - N_{ooo})$$

Donde:

$\Delta_{tot}$ : La variación total entre los dos periodos analizados.

$\Delta_{riesgo}$ : El cambio en función del riesgo.

$\Delta_{pop}$ : Es el cambio en función de los cambios en el tamaño y estructura de la población.

$N_{ooo}$ : El número de casos observados.

$N_{fff}$ : El número de casos previstos.

$N_{off}$ : es el número de casos previstos utilizando la tasa del periodo observado respecto a la población del último periodo previsto.

Este estudio fue aprobado por el Comité Institucional de Ética en Investigación de la Universidad Científica del Sur (CIEI-CIENTÍFICA) (449-2021-POS50).

## Resultados

**La Figura 1** muestra las tasas de mortalidad por cáncer de mama para el último año disponible

y su predicción para el año 2030 en los países de ALC. En 2017, Argentina (19,7), Uruguay (20,2) y Venezuela (17,3) tuvieron las tasas de mortalidad más altas para todas las edades, mientras que para el año 2030, Argentina (17,9), Uruguay (15,6) y Venezuela (17,7) seguirán teniendo las tasas de mortalidad más altas de la región.

En la tabla 1 se presenta la variación porcentual anual estimada de las tasas de mortalidad por cáncer de mama ajustadas por edad en los países de ALC. Diez países mostraron aumentos significativos en sus tasas de mortalidad, siendo los más notables: Colombia (+1.3%), Ecuador, (+1.4%), El Salvador (+2.4), Guatemala (+2.5%), Nicaragua (+2.8%), Panamá (+1.2%), Paraguay (+1.8%), y Venezuela (+1.5%), mientras que Argentina (-1,0%), Chile (-1,6%) y Uruguay (-1,2%) reportaron tendencias a la baja durante el periodo de estudio (Figura 2 y Figura 3). Estas variaciones también fueron similares en la mayoría de los países de ALC utilizando la población de Segi, sin embargo, se pudo apreciar que las tasas de mortalidad si fueron menores (Tabla suplementaria 1)

En las mujeres menores de 40 años, las tasas de mortalidad por cáncer de mama en Cuba (-2,3%), México (-1,0%), y Uruguay (-1,9%) disminuyeron significativamente, mientras que Brasil (+1,5%), Colombia (+1,2%), Guatemala (+3,6%) y Venezuela (+1,1%) mostraron aumentos significativos durante el periodo de estudio (Tabla 2, Figura 2 y Figura 3).

En las mujeres de 40 a 59 años, ocho países presentaron reducciones significativas en sus tasas de mortalidad, siendo las más notables Argentina (-1,2%), Costa Rica (-1,4%), Cuba (-1,5%), Puerto Rico (-1,3%), y Uruguay (-1,8%). Por otro lado, seis países presentaron aumentos significativos en sus tasas de mortalidad, teniendo como principales países a El Salvador (2,9%), Guatemala (2,8%), Nicaragua (1,4%) y Paraguay (1,5%) (Tabla 3, Figura 2 y Figura 3).

En las mujeres de 60 años y más, las tasas de mortalidad por cáncer de mama disminuyeron

significativamente en Argentina (-0,8%), Chile (-0,7%) y Uruguay (-0,7%), mientras que once países presentaron aumentos significativos, siendo los más representativos Ecuador (+2,2%), Nicaragua (+3,9%), Paraguay (+2,8%) y Venezuela (+2,3%) (Tabla 4, Figura 2 y Figura 3).

Según las predicciones para 2030, en mujeres de todas las edades, la mayoría de los países presentarán aumentos en su mortalidad. Se pronostican que habrá disminuciones en las tasas de mortalidad por cáncer de mama en 5 de los 17 países incluidos, sin embargo, debido al aumento debido al cambio de la población, se pronostican aumentos en la mayoría de los países de América Latina y el Caribe, principalmente en Guatemala (+63,0%), Nicaragua (+47,3), El Salvador (+46,2%), Ecuador (+38,5%) y Venezuela (+29,9%) (Tabla 5).

## **Discusión**

En este estudio, algunos países de ALC registraron aumentos en las tasas de mortalidad por cáncer de mama de más del 2% anual, mientras que otros notificaron disminuciones del 1% al 1,6%. Entre 1997 y 2017, los patrones de mortalidad por cáncer de mama variaron de manera significativa en los países de ALC dependiendo del grupo etario seleccionado. Además, se espera que todos los países de ALC presenten aumentos en la mortalidad por cáncer de mama para el año 2030.

Encontramos que entre 1997 y 2017 Argentina, Uruguay y Venezuela tuvieron las tasas de mortalidad por cáncer de mama más altas de la región. Estos resultados reflejan las tendencias actuales reportadas por GLOBOCAN para el año 2020, que indican que estos tres países tuvieron las tasas más altas de la región (más de 17 muertes por 100,000) [1, 3]. No obstante, estas tasas son bajas en comparación con países que no se han incluido en este estudio, como Barbados, Jamaica y Bahamas, que registran tasas mayores a 30 muertes por cada 100.000

habitantes [3]. Estas tasas sólo son comparables a las de los países africanos, que registran tasas superiores a 20 muertes por 100.000. Una de las principales diferencias en la mortalidad entre los países mencionados podrían explicarse por las variaciones en las estrategias de prevención, el acceso a los servicios de salud, la cobertura de los seguros médicos y las prácticas de atención al paciente (por ejemplo, la falta de especialistas en las zonas rurales de cada país o de institutos especializados para el manejo integral del cáncer). De hecho, en América Latina se estima que una tercera parte de la población no tiene acceso a atención de salud debido a razones económicas y que una cifra similar renuncia a buscar atención o cumplir su tratamiento debido a las barreras geográficas [13]. Además, algunos estudios reportan que en América Latina el pronóstico de cáncer de mama es peor que en los países desarrollados, debido principalmente al estadio tardío de la enfermedad al diagnóstico, especialmente cuando se une a una inadecuada capacidad del sistema sanitario para lograr un diagnóstico y tratamiento oportuno [14-16].

Las desigualdades en las tasas de mortalidad entre los países de ALC según en grupo etario utilizado en este estudio sigue siendo significativa. Por ejemplo, nuestro estudio reportó que Brasil, Colombia, Guatemala y Venezuela presentaron aumentos significativos en sus tasas de mortalidad para las mujeres jóvenes menores de 40 años. Estos resultados son realmente preocupante, sin embargo, son cifras esperadas debido a la baja supervivencia por esta enfermedad en los países de América Latina [14]. De hecho, varios estudios de ALC han encontrado una fuerte relación entre el diagnóstico de cáncer de mama en fase tardía y la supervivencia [17-19]. Dependiendo de la organización sanitaria de cada país y del seguro médico individual, el estatus socioeconómico podría influir en el acceso a la asistencia (incluido el acceso al diagnóstico precoz y al tratamiento con fármacos específicos) [20], lo que permitiría ser diagnosticadas en una fase más temprana, lo que mejoraría sus posibilidades de supervivencia [21]. Por tal motivo, es necesario invertir más en los sistemas sanitarios de los



países de ALC para detectar precozmente el cáncer de mama, diagnosticarlo antes y ofrecer un tratamiento accesible y barato a todas las mujeres.

Para el año 2021 se creó la Iniciativa Mundial contra el Cáncer de Mama de la OMS, con el objetivo de reducir el cáncer de mama en un 2,5% anual [9]. Sin embargo, nuestro estudio reportó un aumento de la mortalidad por cáncer de mama en todos los países de ALC para el año 2030, principalmente en países como Argentina, Brasil, Paraguay, Uruguay y Venezuela, quienes tendrán las tasas de mortalidad más altas, con más de 12 muertes por cada 100,000. Además, la mayoría de los países latinoamericanos migrarán hacia una estructura de edad de la población más avanzada, lo que provocará una transición epidemiológica. Por tal motivo. Es importante enfocarse en la promoción de la salud para la detección precoz, un diagnóstico rápido en menos de 60 días y una gestión del cáncer de mama como servicios y tratamientos centralizados con el objetivo de alcanzar el 80% de mujeres que cumplan el tratamiento de manera completa.

Este estudio presenta las limitaciones habituales de un análisis de un registro de cáncer de una base de datos secundaria, como son la calidad y validez de la certificación de las muertes, la falta de información específica sobre las características del tumor, la información limitada a nivel individual y la falta de casos para poder realizar un análisis de incidencia y mostrar un análisis más completo de lo que está ocurriendo en relación con el cáncer de mama en cada país de ALC. Además, es importante resaltar las diferencias en cuanto a la calidad en los registros de datos de mortalidad, lo cual pueden generar diferencias al momento de realizar comparaciones entre las tasas de mortalidad. Por tal motivo, es importante promover una mejor información a partir de datos fiables que procedan de los países de la región.

## **Conclusión**

Este es el primer estudio que analiza las tasas de mortalidad por cáncer de mama de 1997 a 2017, con proyecciones hacia el año 2030 en diecisiete países de ALC. Se reportó una heterogeneidad en la evolución de las tasas de mortalidad por cáncer de mama según país y grupo etario. Se espera que para el 2030, la mortalidad por cáncer de mama aumente en todos los países de ALC, esto principalmente por el cambio en la estructura y tamaño poblacional. Para alcanzar los objetivos de reducir la mortalidad por cáncer de mama, los países de ALC deberán implementar estrategias de salud pública como la promoción de la salud y detección precoz; diagnóstico oportuno; y tratamiento integral de esta neoplasia.

### **Declaraciones**

#### **Aprobación ética y consentimiento para participar**

Este estudio fue aprobado por el Comité Institucional de Ética en Investigación de la Universidad Científica del Sur (CIEI-CIENTÍFICA) (449-2021-POS50).

#### **Consentimiento para la publicación**

No aplicable para este estudio

#### **Disponibilidad de datos y materiales**

Los conjuntos de datos generados y/o analizados durante el presente estudio están disponibles en el siguiente enlace: <https://www.who.int/data/data-collection-tools/who-mortality-database>

#### **Conflicto de intereses**

Los autores declaran no tener conflicto de intereses.

#### **Fuente de financiación**

Este trabajo de investigación ha sido financiado por la Universidad Científica del Sur (Concurso de fondos Beca Cabieses, Resolución Directoral N° 011-DGIDI-CIENTÍFICA-2021).

#### **Contribución de los autores**

Concepción y diseño de la idea: JSTR, JYM.

Tuvieron pleno acceso a todos los datos del estudio y asumen la responsabilidad de la integridad de los datos y la exactitud del análisis de los mismos: JSTR, SL.

Contribuyeron a la redacción del manuscrito: Todos los autores.

Contribuyeron al análisis estadístico: JSTR, BV.

Revisión crítica del manuscrito: CSA, YHR.

Aprobación de la versión presentada y final: Todos los autores.

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Figura 1. Tasas de mortalidad por cáncer de mama para 1997 y 2017 en los países de América Latina y el Caribe.

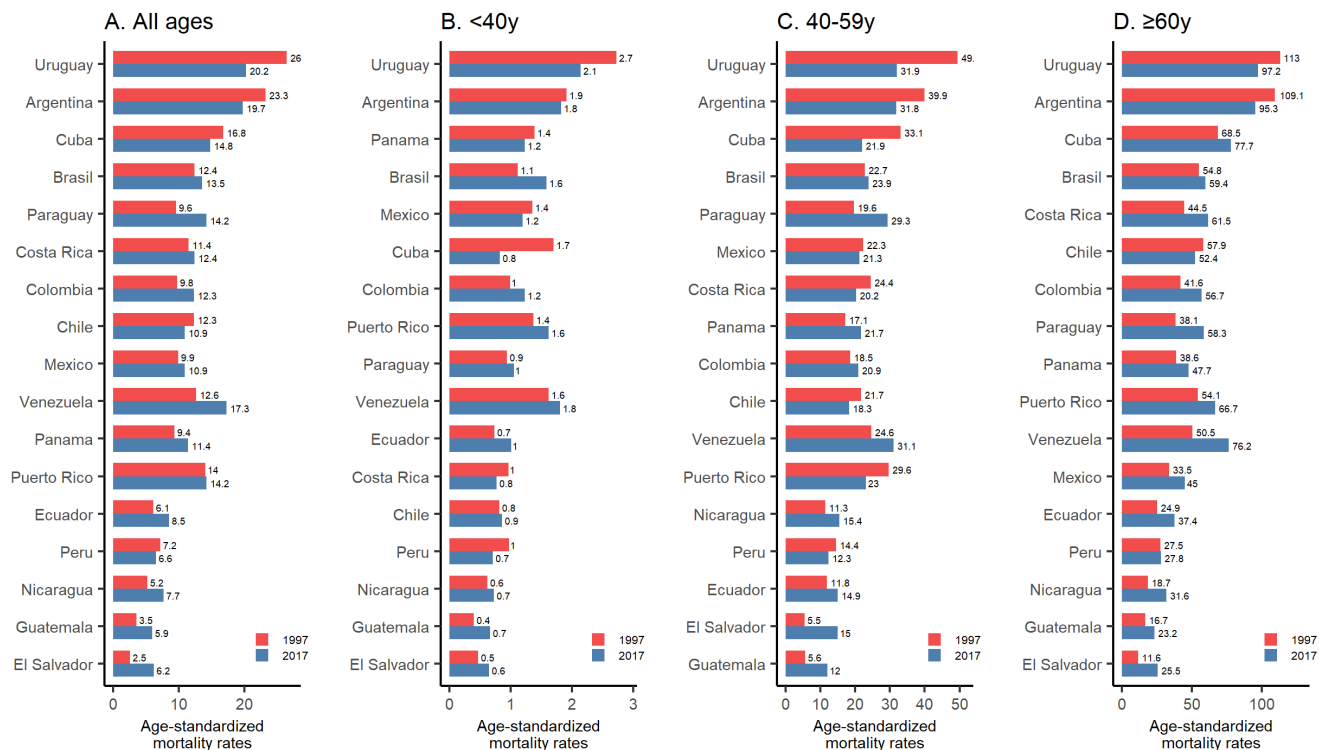


Figura 2. Evolución de las tasas de mortalidad por cáncer de mama en mujeres de América Latina y el Caribe, 1997 al 2017.

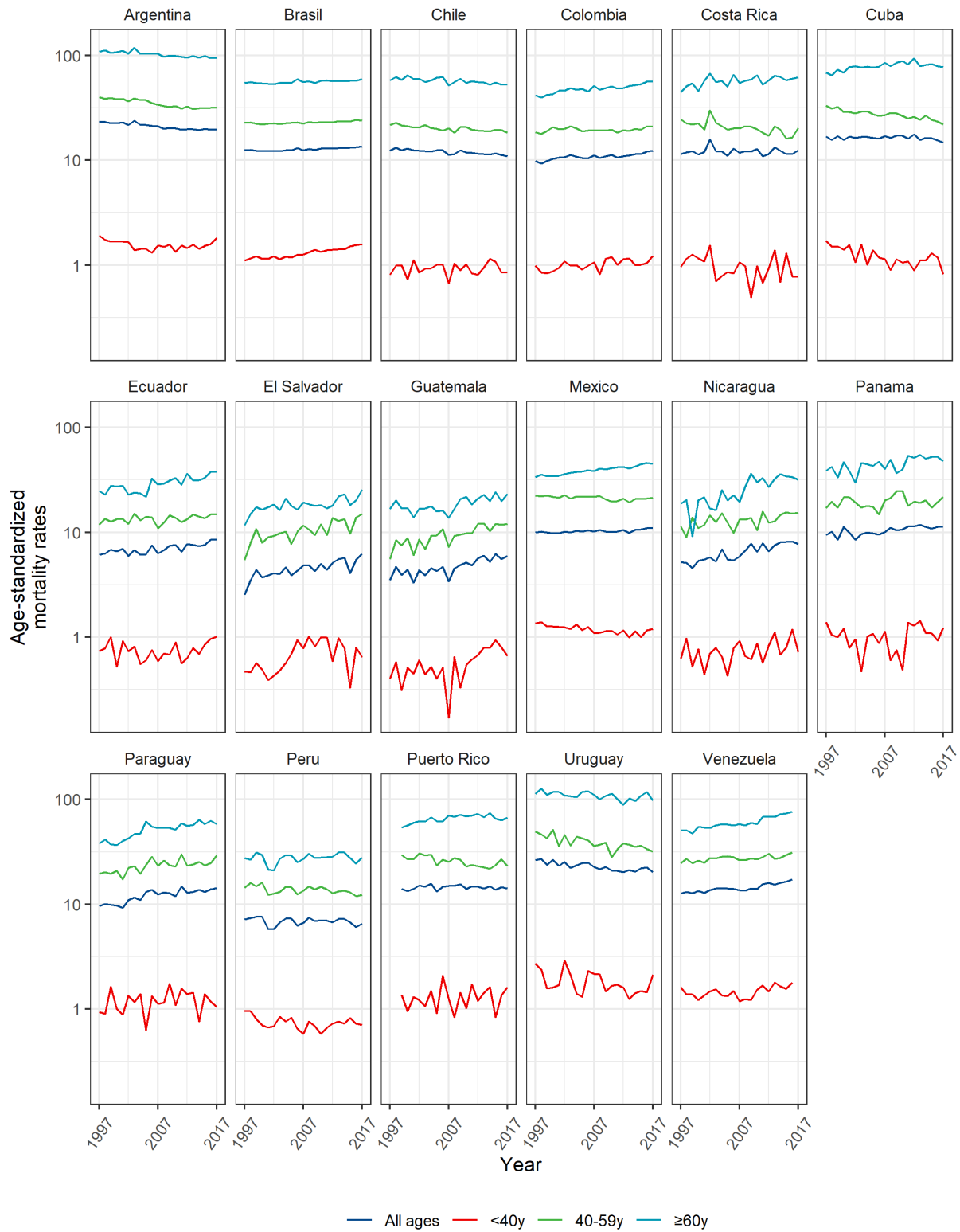


Figura 3. Cambio porcentual anual promedio de las tasas de mortalidad por cáncer de mama en mujeres de América Latina y el Caribe, 1997 al 2017.

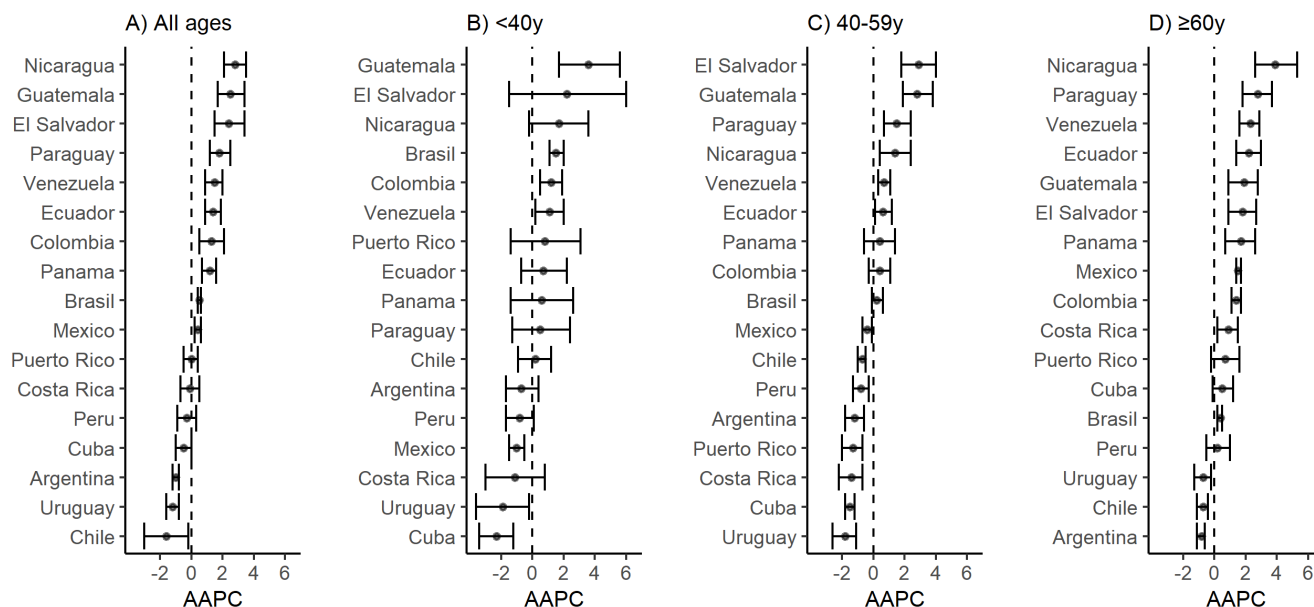


Tabla 1. Cambio porcentual anual promedio (CPAP) con sus intervalos de confianza del 95% (IC95%) para las tasas de mortalidad por cáncer de mama ajustadas por edad (WHO standard population) entre mujeres de todas las edades en América Latina y el Caribe, 1997-2017.

Países	Años	CPA	Años	CPA	Años	CPA	CPAP
Argentina	1997-2017	-1.0(-1.2, -0.8)*					-1.0(-1.2, -0.8)*
Brasil	1997-2017	0.5(0.4-0.6)*					0.5(0.4-0.6)*
Chile	1997-2017	-0.7(-0.9, -0.5)*					-0.7(-0.9, -0.5)*
Colombia	1997-2002	2.7(0.2,5.3)*	2002-2013	0(-0.7, 0.7)	2013-2017	2.5(0.8,4.2)*	1.3(0.5,2.1)*
Costa Rica	1997-2017	-0.1(-0.7, 0.5)					
Cuba	1997-2012	0.2(-0.2, 0.6)	2012-2017	-2.3(-4.2, -0.3)*			-0.4(-0.9, 0.2)
Ecuador	1997-2017	1.4(0.9-1.9)*					1.4(0.9-1.9)*
El Salvador	1997-2017	2.4(1.5, 3.4)*					2.4(1.5, 3.4)*
Guatemala	1997-2017	2.5(1.7-3.4)*					2.5(1.7-3.4)*
México	1997-2017	0.4(0.2-0.6)*					0.4(0.2-0.6)*
Nicaragua	1997-2017	2.8(2.1-3.5)*					2.8(2.1-3.5)*
Panamá	1997-2017	1.1(0.6-1.5)*					1.1(0.6-1.5)*
Paraguay	1997-2017	1.9(1.3-2.5)*					1.9(1.3-2.5)*
Perú	1997-2017	-0.3(-0.9, 0.3)					-0.3(-0.9, 0.3)
Puerto Rico	1999-2017	-0(-0.4, 0.4)					-0(-0.4, 0.4)
Uruguay	1997-2017	-1.2(-1.6, -0.8)*					-1.2(-1.6, -0.8)*
Venezuela	1997-2009	0.8(0.1,1.4)*	2009-2016	2.7(1.6,3.9)*			1.5(0.9,2.0)*

\* valor p <0,05; CPA: Cambio porcentual anual; CPAP: Cambio porcentual anual promedio

Tabla 2. Cambio porcentual anual promedio (CPAP) con sus intervalos de confianza del 95% (IC95%) para las tasas de mortalidad por cáncer de mama ajustadas por edad (WHO standard population) entre menores de 40 años en América Latina y el Caribe, 1997-2017.

Países	Años	CPA	Años	CPA	CPAP
Argentina	1997-2005	-3.6*(-5.8,-1.4)	2005-2017	1.4*(0.2,2.5)	-0.7(-1.7,0.4)
Brasil	1997-2003	0.3(-1.2,1.8)	2003-2017	2.1*(1.7,2.4)	1.5*(1.1,2.0)
Chile	1997-2017	0.2(-0.9,1.2)			0.2(-0.9,1.2)
Colombia	1997-2017	1.2*(0.5,1.9)			1.2*(0.5,1.9)
Costa Rica	1997-2017	-1.1(-3.0,0.8)			-1.1(-3.0,0.8)
Cuba	1997-2017	-2.3*(-3.4,-1.2)			-2.3*(-3.4,-1.2)
Ecuador	1997-2017	0.7(-0.7,2.2)			0.7(-0.7,2.2)
El Salvador	1997-2010	7.1*(3.0,11.4)	2010-2017	-6.4(-14.2,2.1)	2.2(-1.5,6.0)
Guatemala	1997-2017	3.6*(1.7,5.6)			3.6*(1.7,5.6)
Mexico	1997-2017	-1.0*(-1.5,-0.5)			-1.0*(-1.5,-0.5)
Nicaragua	1997-2017	1.7(-0.2,3.6)			1.7(-0.2,3.6)
Panama	1997-2017	0.6(-1.4,2.6)			0.6(-1.4,2.6)
Paraguay	1997-2017	0.5(-1.3,2.4)			0.5(-1.3,2.4)
Peru	1997-2017	-0.8(-1.7,0.1)			-0.8(-1.7,0.1)
Puerto Rico	1997-2017	0.8(-1.4,3.1)			0.8(-1.4,3.1)
Uruguay	1997-2017	-1.9*(-3.6,-0.2)			-1.9*(-3.6,-0.2)
Venezuela	1997-2016	1.1*(0.2,2.0)			1.1*(0.2,2.0)

\* valor p <0,05

CPA: Cambio porcentual anual

CPAP: Cambio porcentual anual promedio



Tabla 3. Cambio porcentual anual promedio (CPAP) con sus intervalos de confianza del 95% (IC95%) para las tasas de mortalidad por cáncer de mama ajustadas por edad (WHO standard population) entre 40 a 59 años en América Latina y el Caribe, 1997-2017.

Países	Años	CPA	Años	CPA	CPAP
Argentina	1997-2013	-1.7*(-2.0,-1.3)	2013-2017	0.6(-2.2,3.5)	-1.2*(-1.8,-0.6)
Brasil	1997-2000	-1.3(-3.4,0.9)	2000-2017	0.5*(0.3,0.6)	0.2(-0.1,0.6)
Chile	1997-2017	-0.7*(-1.0,-0.5)			-0.7*(-1.0,-0.5)
Colombia	1997-2013	-0.1(-0.6,0.4)	2013-2017	2.3(-0.9,5.7)	0.4(-0.3,1.1)
Costa Rica	1997-2017	-1.4*(-2.2,-0.7)			-1.4*(-2.2,-0.7)
Cuba	1997-2017	-1.5*(-1.8,-1.2)			-1.5*(-1.8,-1.2)
Ecuador	1997-2017	0.6*(0.1,1.2)			0.6*(0.1,1.2)
El Salvador	1997-2017	2.9*(1.8,4.0)			2.9*(1.8,4.0)
Guatemala	1997-2017	2.8*(1.9,3.8)			2.8*(1.9,3.8)
Mexico	1997-2017	-0.4*(-0.7,-0.1)			-0.4*(-0.7,-0.1)
Nicaragua	1997-2017	1.4*(0.4,2.4)			1.4*(0.4,2.4)
Panama	1997-2017	0.4(-0.6,1.4)			0.4(-0.6,1.4)
Paraguay	1997-2017	1.5*(0.7,2.4)			1.5*(0.7,2.4)
Peru	1997-2017	-0.8*(-1.3,-0.3)			-0.8*(-1.3,-0.3)
Puerto Rico	1997-2017	-1.3*(-2.0,-0.7)			-1.3*(-2.0,-0.7)
Uruguay	1997-2017	-1.8*(-2.6,-1.1)			-1.8*(-2.6,-1.1)
Venezuela	1997-2016	0.7*(0.3,1.1)			0.7*(0.3,1.1)

\* valor p <0,05

CPA: Cambio porcentual anual

CPAP: Cambio porcentual anual promedio

Tabla 4. Cambio porcentual anual promedio (CPAP) con sus intervalos de confianza del 95% (IC95%) para las tasas de mortalidad por cáncer de mama ajustadas por edad (WHO standard population) entre mujeres  $\geq 60$  años en América Latina y el Caribe, 1997-2017.

Países	Años calendarios	APC	Año Calendario	APC	AAPC
Argentina	1997-2017	-0.8*(-1.1,-0.6)			-0.8*(-1.1,-0.6)
Brasil	1997-2017	0.4*(0.2,0.5)			0.4*(0.2,0.5)
Chile	1997-2017	-0.7*(-1.1,-0.4)			-0.7*(-1.1,-0.4)
Colombia	1997-2017	1.4*(1.1,1.7)			1.4*(1.1,1.7)
Costa Rica	1997-2017	0.9*(0.2,1.5)			0.9*(0.2,1.5)
Cuba	1997-2012	1.6*(1.1,2.2)	2012-2017	-2.6*(-4.9,-0.3)	0.5*(-0.1,1.2)
Ecuador	1997-2017	2.2*(1.4,3.0)			2.2*(1.4,3.0)
El Salvador	1997-2017	1.8*(0.9,2.7)			1.8*(0.9,2.7)
Guatemala	1997-2017	1.9*(0.9,2.8)			1.9*(0.9,2.8)
Mexico	1997-2017	1.5*(1.4,1.7)			1.5*(1.4,1.7)
Nicaragua	1997-2017	3.9*(2.6,5.3)			3.9*(2.6,5.3)
Panama	1997-2017	1.7*(0.7,2.6)			1.7*(0.7,2.6)
Paraguay	1997-2005	5.2*(2.9,7.5)	2005-2017	1.2*(0.3,2.1)	2.8*(1.8,3.7)
Peru	1997-2017	0.2(-0.5,1.0)			0.2(-0.5,1.0)
Puerto Rico	1997-2012	1.9*(1.1,2.7)	2012-2017	-2.4(-5.3,0.5)	0.7(-0.2,1.6)
Uruguay	1997-2017	-0.7*(-1.3,-0.2)			-0.7*(-1.3,-0.2)
Venezuela	1997-2016	2.3*(1.6,2.9)			2.3*(1.6,2.9)

\* valor  $p < 0,05$

CPA: Cambio porcentual anual

CPAP: Cambio porcentual anual promedio

Tabla 5. Número de defunciones por cáncer de mama, tasas de mortalidad estandarizadas por edad y cambio porcentual de los casos debido al crecimiento de la población y al riesgo entre las mujeres de América Latina y el Caribe, 2017 y predicción para 2030. (todas las edades).

Country	Female population (million per year)		Number of deaths in women of all ages		Age-standardized mortality rates		Total change, %	Change due to population, %	Change due to risk, %
	2017	2030	2017	2030	2017	2030			
Argentina	22.60	25.07	6024	7421	17.52	17.92	27.9	26.7	1.2
Brazil	107.44	114.24	16723	25368	12.10	13.09	65.1	50.6	14.5
Chile	9.28	9.85	1504	1904	9.73	9.56	30.1	37.7	-7.5
Colombia	24.93	27.22	3300	5151	10.89	11.41	75.1	58.9	16.3
Costa Rica	2.45	2.74	366	593	10.90	11.67	76.9	63.6	13.3
Cuba	5.67	5.62	1519	1699	12.96	11.17	12.0	30.8	-18.8
Ecuador	8.32	9.92	667	1144	7.60	8.70	97.7	59.2	38.5
El Salvador	3.25	3.62	217	220	6.22	6.89	87.1	40.9	46.2
Guatemala	8.68	10.74	352	739	5.35	7.08	129.9	66.8	63.0
México	65.44	71.96	6755	9746	9.93	9.74	58.2	52.8	5.5
Nicaragua	3.15	3.75	202	410	7.00	9.04	112.6	65.3	47.3
Panamá	2.02	2.47	241	508	10.18	11.09	129.4	107.0	22.4
Paraguay	3.36	3.92	391	556	12.78	12.32	56.8	53.8	3.0
Perú	16.10	18.16	1030	1517	5.86	5.74	52.4	58.4	-6.0
Puerto Rico	1.91	1.53	445	492	12.51	11.35	13.0	19.4	-6.4
Uruguay	1.79	1.84	204	260	17.91	15.60	7.0	23.4	-16.4
Venezuela	16.54	17.06	2513	1289	15.58	17.65	77.5	47.6	29.9

Tabla suplementaria 1. Cambio porcentual anual promedio (CPAP) con sus intervalos de confianza del 95% (IC95%) para las tasas de mortalidad por cáncer de mama ajustadas por edad (Segi population) entre mujeres de todas las edades en América Latina y el Caribe, 1997-2017.

Países	Años	CPA	Años	CPA	Años	CPA	CPAP
Argentina	1997-2017	-1.0*(-1.2,-0.8)					-1.0*(-1.2,-0.8)
Brasil	1997-2017	0.5*(0.4, 0.6)					0.5*(0.4, 0.6)
Chile	1997-2017	-1.6*(-3.0, -0.2)					-1.6*(-3.0, -0.2)
Colombia	1997-2002	2.7*(0.2, 5.3)	2002-2013	0(-0.7, 0.7)	2013-2017	3.0*(0.5, 5.5)	1.3*(0.5, 2.1)
Costa Rica	1997-2017	-0.1(-0.7, 0.5)					-0.1(-0.7, 0.5)
Cuba	1997-2012	0.2(-0.2, 0.6)	2012-2017	-2.4*(-4.2, -0.6)			-0.5(-1.0, 0)
Ecuador	1997-2017	1.4*(0.9, 1.9)					1.4*(0.9, 1.9)
El Salvador	1997-2017	2.4*(1.5, 3.4)					2.4*(1.5, 3.4)
Guatemala	1997-2017	2.5*(1.7, 3.4)					2.5*(1.7, 3.4)
Mexico	1997-2017	0.4*(0.2, 0.6)					0.4*(0.2, 0.6)
Nicaragua	1997-2017	2.8*(2.1, 3.5)					2.8*(2.1, 3.5)
Panama	1997-2017	1.2*(0.7, 1.6)					1.2*(0.7, 1.6)
Paraguay	1997-2017	1.8*(1.2, 2.5)					1.8*(1.2, 2.5)
Peru	1997-2017	-0.3(-0.9, 0.3)					-0.3(-0.9, 0.3)
Puerto Rico	1999-2017	0(-0.5, 0.4)					0(-0.5, 0.4)
Uruguay	1997-2017	-1.2*(-1.6, -0.8)					-1.2*(-1.6, -0.8)
Venezuela	1997-2009	0.8*(0.1, 1.4)	2009-2016	2.7*(1.6, 3.9)			1.5*(0.9, 2.0)

Abreviaturas.

ALC: América Latina y el Caribe

OMS: Organización Mundial de la Salud

CPA: Cambio porcentual anual

CPAM: Cambio porcentual anual promedio

Anexos:

Pueden encontrar esta tesis como publicación en el siguiente enlace:

<https://bmcpublihealth.biomedcentral.com/articles/10.1186/s12889-023-16328-w>

Torres-Román *et al.* *BMC Public Health* (2023) 23:1449  
<https://doi.org/10.1186/s12889-023-16328-w>

BMC Public Health

RESEARCH

Open Access

## Disparities in breast cancer mortality among Latin American women: trends and predictions for 2030



J. Smith Torres-Román<sup>1\*</sup>, Jorge Ybaseta-Medina<sup>2,3</sup>, Silvana Loli-Guevara<sup>2,4</sup>, Janina Bazalar-Palacios<sup>5</sup>, Bryan Valcarcel<sup>2</sup>, Miguel A. Arce-Huamani<sup>1,2</sup>, Christian S Alvarez<sup>2</sup> and Yamilee Hurtado-Roca<sup>1</sup>

### Abstract

**Background** Breast cancer is among the leading cause of cancer-related mortality among Latin American and Caribbean (LAC) women, but a comprehensive and updated analysis of mortality trends is lacking. The objective of this study was to determine the breast cancer mortality rates between 1997 and 2017 for LAC countries and predict mortality until 2030.

**Methods** We retrieved breast cancer deaths across 17 LAC countries from the World Health Organization mortality database. Age-standardized mortality rates per 100,000 women-years were estimated. Mortality trends were evaluated with Joinpoint regression analyses by country and age group (all ages, < 50 years, and ≥ 50 years). By 2030, we predict number of deaths, mortality rates, changes in population structure and size, and the risk of death from breast cancer.

**Results** Argentina, Uruguay, and Venezuela reported the highest mortality rates throughout the study period. Guatemala, El Salvador, and Nicaragua reported the largest increases (from 2.4 to 2.8% annually), whereas Argentina, Chile, and Uruguay reported downward trends (from -1.0 to -1.6% annually). In women < 50y, six countries presented downward trends and five countries showed increasing trends. In women ≥ 50y, three countries had decreased trends and ten showed increased trends. In 2030, increases in mortality are expected in the LAC region, mainly in Guatemala (+63.0%), Nicaragua (+47.3), El Salvador (+46.2%), Ecuador (+38.5%) and Venezuela (+29.9%).

**Conclusion** Our findings suggest considerable differences in breast cancer mortality across LAC countries by age group. To achieve the 2030 sustainable developmental goals, LAC countries should implement public health strategies to reduce mortality by breast cancer.

**Keywords** Breast cancer, Mortality, Latin America, Caribbean Region, Forecasting

La base de datos pueden descargarlo del siguiente enlace:  
<https://www.who.int/data/data-collection-tools/who-mortality-database>

## Aprobación del comité de ética

COMITÉ INSTITUCIONAL DE ÉTICA EN  
 INVESTIGACIÓN



### CONSTANCIA N° 307-CIEI-CIENTÍFICA-2021

El presidente del Comité Institucional de Ética en Investigación de la Universidad Científica del Sur (CIEI-CIENTÍFICA) da constancia que el proyecto de investigación, cuyos datos se registran a continuación, ha sido aprobado por el CIEI-CIENTÍFICA.

Código de registro: **449-2021-POS50**

Título: **Evolución de las tasas de mortalidad por cáncer de mama en países latinoamericanos y su mortalidad para el año 2030**

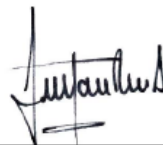
Investigador(a): **Junior Smith Torres Román**

La aprobación del proyecto de investigación implica que el documento presentado a evaluación cumple con los lineamientos de Universidad en materia de investigación y ética, los cuales se sustentan en la normativa internacional vigente. Adicionalmente, en el contexto de la pandemia de enfermedad por COVID-19, le recomendamos cumplir con las normas publicadas por el estado peruano (accesos, medidas de bioseguridad, etc.) y tener los permisos de las instituciones en las que realizará el estudio antes de ejecutarlo.

En tal sentido, esta aprobación carecerá de valor si es que el proyecto de investigación arriba indicado es modificado de cualquier forma. Toda enmienda, añadido, eliminación o eventualidad (eventos adversos, etc.) posterior a la fecha de aprobación debe ser reportado al CIEI-CIENTÍFICA.

La vigencia de la aprobación de este documento es de dieciocho (18) meses (hasta el 19 de febrero del 2023), periodo en el que puede desarrollarse el proyecto. Cualquier trámite para su renovación deberá ser enviado antes del término de la vigencia de este documento, debiendo suspenderse todo desarrollo hasta que la renovación sea aprobada. La presente aprobación será ratificada en la sesión del CIEI más próxima.

Villa El Salvador, 20 de agosto de 2021




Mg. Fulton Paul Rivera Albinagorta  
 Presidente  
 Comité Institucional de Ética en Investigación

## Constancia de Renovación\_449-2021-POS50

COMITÉ INSTITUCIONAL DE ÉTICA EN  
INVESTIGACIÓN



### Constancia

Luego de la revisión de la solicitud, el presidente del Comité Institucional de Ética en Investigación de la Universidad Científica del Sur (CIEI-CIENTÍFICA) hace constar que el CIE-CIENTÍFICA ha aprobado de forma expedita la **renovación** del proyecto de investigación que se detalla continuación:

Código de registro: **449-2021-POS50**

Título: **"Evolución de las tasas de mortalidad por cáncer de mama en países latinoamericanos y su mortalidad para el año 2030"**

Investigador(es): **Junior Smith Torres Roman**

Constancia de aprobación: **CONSTANCIA N° 307-CIEI-CIENTÍFICA-2021**

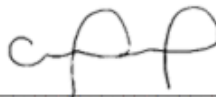
Por consiguiente, se otorga:

**Renovación de vigencia del periodo de aprobación ética.** Vista la solicitud, **se renueva** la vigencia de la aprobación ética por un periodo de seis meses; es decir, hasta el **29 de diciembre del 2023**. El proyecto solo podrá ejecutarse entre los periodos detallados en este documento y el **investigador** tendrá que realizar la solicitud de una nueva ampliación 30 días antes de finalizar esta renovación de la aprobación.

Dejando constancia que hay un periodo de ventana (entre el 19 de febrero del 2023 hasta el 30 de junio de 2023) que toda actividad de investigación estuvo suspendida, sin el amparo del comité.

Todas las demás características de la investigación descritas en el proyecto original permanecen; por lo que cualquier otra modificación deberá informarse a este Comité, para su evaluación.

Lima, 30 de junio de 2023



Mg. Cinthya Ruth Chipana Herquinio  
Presidente

Comité Institucional de Ética en Investigación

## Resolución Directoral Académica de Medicina Humana.



### RESOLUCIÓN DIRECTORAL ACADÉMICA DE CARRERA No. 603 - DACMH-DAFCS-U. CIENTÍFICA-2021

Lima, 10 de setiembre del 2021

#### VISTO:

El informe de revisión independiente académica y la aprobación de un Comité de Ética del proyecto de investigación titulado: "EVOLUCIÓN DE LAS TASAS DE MORTALIDAD DE CÁNCER DE MAMA EN PAÍSES LATINOAMERICANOS Y SU MORTALIDAD PARA EL AÑO 2030".

#### CONSIDERANDO:

Que, de acuerdo al Reglamento General de la Universidad Científica del Sur y el reglamento y Procedimientos de trabajos de Investigación para obtener el Grado de Maestro.

Que, de acuerdo a la normativa vigente de la Universidad Científica del Sur, en uso de las atribuciones conferidas al Director Académico de la Carrera.

#### SE RESUELVE:

**ART. 1°** Aprobar, en vías de regularización e inscribir el proyecto de tesis titulado "EVOLUCIÓN DE LAS TASAS DE MORTALIDAD DE CÁNCER DE MAMA EN PAÍSES LATINOAMERICANOS Y SU MORTALIDAD PARA EL AÑO 2030", presentado por el alumno JUNIOR SMITH TORRES ROMÁN con N° de registro: 449-2021-POSS0.

**ART. 2°** Nombrar la Docente Leda Yamilee Hurtado Roca, como asesor para el desarrollo de la tesis en cuestión.

Regístrese, comuníquese y archívese.




Mg. JORDI GRAU MONGE  
 Director Académico (e)  
 Carrera de Medicina Humana

c.c. Archivo



## Resolución Directoral Académica de Medicina Humana (Renovación)

RESOLUCIÓN DIRECTORAL ACADÉMICA DE CARRERA No. 414- DACMH-DAFCS-U. CIENTÍFICA-  
2023

Villa el Salvador, 10 de julio del 2023

## VISTO:

El informe de revisión independiente académica y la aprobación de un Comité de Ética del proyecto de investigación titulado: "EVOLUCIÓN DE LAS TASAS DE MORTALIDAD POR CÁNCER DE MAMA EN PAÍSES LATINOAMERICANOS Y SU MORTALIDAD PARA EL AÑO 2030".

## CONSIDERANDO:

Que, de acuerdo al Reglamento General de la Universidad Científica del Sur y el reglamento y Procedimientos de trabajos de Investigación para obtener el **Grado de Maestro**.

Que, de acuerdo a la normativa vigente de la Universidad Científica del Sur, en uso de las atribuciones conferidas al Director Académico de la Carrera.

## SE RESUELVE:

**ART. 1° Aprobar**, en vías de regularización e inscribir el proyecto de tesis titulado "EVOLUCIÓN DE LAS TASAS DE MORTALIDAD POR CÁNCER DE MAMA EN PAÍSES LATINOAMERICANOS Y SU MORTALIDAD PARA EL AÑO 2030", presentado por el alumno: Junior Smith Torres Román con N° de registro: 449-2021-POS50.

**ART. 2° Nombrar** al Docente **Leda Yamilee Hurtado Roca** como asesor para el desarrollo de la tesis en cuestión.

Regístrese, comuníquese y archívese.



Mg. JORDI GRAU MONGE  
Director Académico (e)  
Carrera de Medicina Humana