Breast cancer survival in Mexico between 2007 and 2016 in women without social security: a retrospective cohort study

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Summary

Background Essential indicators of health system performance for breast cancer are lacking in Mexico. We estimated survival and clinical stage distribution for women without social insurance who were treated under a health financing scheme that covered 60% of the Mexican population.

Methods We conducted a retrospective cohort study cross-linking reimbursement claims for 56,847 women treated for breast cancer between 2007 and 2016 to a mortality registry. We estimated overall- and clinical stage-specific survival and breast cancer survival according to patient age, state of residence, marginalization, type of treatment facility, and patient volume of the treatment facility. We also explored the distribution of clinical stage according to age, year of treatment initiation, and state where the woman was treated. We used log-rank tests and estimated 95% CIs to compare differences between patient groups.

Findings Median age was 52 years (interquartile range [IQR] 45, 61) (Sixty five percent patients (36,731/56,847) had advanced disease at treatment initiation. Five-year overall survival was 72.2% (95% CI 71.7, 72.6). For early disease (excluding stage 0), 5-year overall survival was 89.0% (95% CI 88.4, 89.5), for locally advanced disease 69.9% (95% CI 69.0, 70.2) and for metastatic 36.9% (95% CI 35.4, 38.4). Clinical stage at treatment initiation and breast cancer survival remained unchanged in the period analyzed. Clinical stage and survival differed across age groups, state of residence, and type of facility where women received treatment.

Interpretation In the absence of population-based cancer registries, medical claims data may be efficiently leveraged to estimate essential cancer-related performance indicators.

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Keywords: Breast cancer; Survival; Clinical stage; Mexico; Seguro popular

Introduction

Improvements in early detection and access to multimodal treatment have resulted in declines in breast cancer mortality in most high-income countries.[1–3] In contrast, breast cancer mortality remains high in most low- and middle-income countries (LMICs) likely due to late-stage diagnosis and inadequate access to quality care.[4] In Mexico, breast cancer mortality has steadily

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Research in context

Evidence before this study

National breast cancer survival estimates for Mexico are lacking. On August, 2022, we searched PubMed using the search terms ((((breast cancer* OR breast tumor* OR breast tumour* OR breast carcinoma*))) AND (((“stage at diagnosis” or “stage at presentation” or “stage distribution” or “survival”))) AND (Mexico)), without language or publication date restrictions. The only reports on breast cancer stage distributions and survival included patients treated at a few cancer hospitals. We found no nationwide estimates for either breast cancer survival or clinical stage distribution.

Added value of this study

Our study provides the first nationwide clinical stage distribution and survival estimates for breast cancer patients, essential indicators of health system performance for cancer care. Additionally, it shows that cancer stage distribution and survival remained unchanged throughout this 10-year period, despite increased access to cancer treatment. Our assessment comes at a time when Mexico has been implementing a substantial transformation of the health system including a revision of the payment mechanism for high-cost conditions.

Implications of all the available evidence

As countries move towards universal health care, Mexico’s experience in financing cancer treatment may help to broaden the discussion on the selection of key cancer care services to include in universal health coverage packages. Our study findings show how increased access to cancer treatment, although necessary, is not enough to improve survival. Early access to diagnostics is also essential. Additionally, the survival and cancer distribution estimates we obtained can be used to benchmark current and future breast cancer care programs in Mexico. Finally, this study provides a useful example of how in LMICs with low coverage of population-based cancer registries, the linkage of medical claims data from health insurance systems to mortality data may be efficiently leveraged to provide cancer survival estimates.

increased over the last three decades making it the leading cause of cancer death among women.[1]

Clinical stage distribution and survival rates are essential indicators of health system performance in the management of cancer.[5] However, robust estimates for these measures are lacking in Mexico. Given the growing burden of breast cancer in Mexico and the need to expand access to quality breast cancer care, these indicators are key to plan for healthcare improvements and monitor the impact of policies and programs.

Social security in Mexico covers and provides care for individuals working in the formal sector and government and their families. Between 2004 and 2019, *Seguro Popular* financed specific health interventions for the rest of the population (i.e., uninsured and mostly lower income) who comprised approximately 60% of the population. Between 2007 and 2019, breast cancer treatment in Mexico for persons not covered by social security health insurance schemes was financed through *Seguro Popular*.[6] While treatment for this disease was fully covered at no cost (i.e., no co-pay or premium), out-of-pocket expenditure for diagnostic workup was common. In this study, we used nationwide reimbursement claims data for 56,847 incident breast cancer cases among women whose treatment was financed under *Seguro Popular* between 2007 and 2016 to estimate 5-year overall and clinical stage-specific survival, explore patient groups that may be at increased risk for mortality, and describe clinical stage distribution at treatment initiation. We provide estimates that can be used to monitor progress in breast cancer care in Mexico and provide insights for other LMICs on Mexico’s experience with increased public financing for breast cancer treatment.

Materials and methods

Study design and patients

We conducted a retrospective cohort study cross-linking nationwide reimbursement claims data from Mexico’s National Commission for Social Protection in Health (CNPSS, for its Spanish acronym) for breast cancer cases treated between 2007 and 2016, to a national mortality surveillance registry maintained by the Ministry of Health, the System for Epidemiologic Death Statistics (SEED, for its Spanish acronym).[7]

The Mexican health system is a segmented model, where different modalities of financing, service delivery and affiliation coexist, each of them targeting different population groups according to income and type of employment.[8–10] Social security institutions insure employees in the formal sector of the economy (i.e., private company and government employees) and their families and provide services in their own facilities. The uninsured population is entitled to use healthcare services provided by the federal and 32 state Ministries of Health.[11] In addition, there is a large private sector, commonly used by both the uninsured and those insured by Social Security institutions, paying out-of-pocket, to accelerate diagnostic workup and medical care. Between 2004 and 2019, CNPSS implemented *Seguro Popular*. This program financed several health interventions including reimbursement of treatment for high-cost diseases through its Fund for Protection against Catastrophic Expenses. Services were provided mainly through the public health infrastructure that was (and still is) available also for use of the uninsured population. From 2007 to 2018, *Seguro Popular* financed breast cancer treatment based on harmonized guidelines and provided care through hospitals that met

Seguro Popular accreditation requirements.[6] In 2006, 15% of the population was formally covered and 49% was eligible for coverage by *Seguro Popular*.[12] By 2012, the corresponding proportions were 39% and 21%.[13] And finally, in 2018, a year prior to the end of the program, 43% of the Mexican population was formally affiliated to *Seguro Popular* and 15% were eligible.[11] Thus, the proportion of the population either formally covered or eligible remained relatively constant over the period of study. Under this scheme, once the diagnosis of breast cancer was confirmed through biopsy, people could receive treatment at a *Seguro Popular*-accredited facility. Women eligible for the program were often enrolled at the time of diagnosis. While treatment was provided mostly at state and federal public facilities, some private centers were also accredited to provide breast cancer care under this financing mechanism. *Seguro Popular* was eliminated in 2019, and Mexico's national government is currently restructuring the health system.

Between January 2007 and December 2016, we identified 268,703 claims, representing 60,846 patients, submitted to CNPSS for reimbursement. Data for 2017 and 2018 were unavailable. Since claims were submitted by accredited treatment facilities for reimbursement, it is very unlikely that any covered cases would be missing or that uncovered cases would be included in this database. We excluded from our main analyses 3,999 patients: 1,731 in whom staging was not possible (who likely received treatment previous to registration in the CNPSS database), 1,423 recurrent cancer cases, 392 persistent cancer cases, 328 male patients, 84 who had implausible treatment dates, 27 breast sarcomas, and 14 patients with missing identifiers (Supplementary Figure S1). Breast sarcomas (n = 27) and male patients (n = 328) with breast cancers were excluded as they have very different clinical behavior to that of breast carcinomas among females. Thus, our analysis was based on 56,847 women who received initial treatment for breast carcinoma at 63 hospitals accredited by Seguro Popular between 2007 and 2016. This project was approved by the National Institute of Public Health's Institutional Review Board (Project ID 1615).

Procedures

Yearly CNPSS reimbursement datasets between 2007 and 2016 contained personal identifiers (including national identification number, name, date of birth), age, municipality of residence, diagnosis, clinical stage, date of diagnosis, procedure, date of procedure, and facility where treatment occurred. Prior to 2011, accredited treatment facilities submitted one reimbursement claim per patient and received a bundled payment per case. Beginning in 2011, a fee-for-service reimbursement mechanism was established and multiple claims per individual could be submitted by treating hospitals. We harmonized yearly reimbursement datasets to create our analytic dataset which included patients' national identification numbers (or CURP for its Spanish acronym), first and two last names, state and municipality of residence, year of birth, facility and date of initial treatment, and clinical stage.

We categorized women according to age, municipality of residence, clinical stage, year of treatment initiation, and treatment facility. We classified participants according to a widely used geographically defined marginalization index for Mexican municipalities (the 2010 *Índice de Marginación*) that can serve as a proxy for socioeconomic status. Briefly, the index is calculated yearly by Mexico's National Council on Population and Housing (CONAPO, for its acronym in Spanish) using information on household characteristics, education, income, and population size of all municipalities in Mexico.[11] Women who lived in highly and very highly marginalized communities were defined as living in a marginalized area. We categorized the clinical cancer stage reported at patient registration in the FPGC database as: *in situ* (stage 0), early stage (I–IIA), locally-advanced (IIB–IIIC), and metastatic disease (IV). Women were classified by the facility where they received treatment: location relative to residence (i.e., in state or out-of-state), funding (i.e., federally or state funded), and volume of patients treated for breast cancer in the previous year (<148 for low volume, 148–298 for medium volume, and >298 for high volume).[12]

We cross-linked study participants to deaths reported in SEED between January 2007 and December 2017. SEED is a mortality registry designed for disease surveillance that is maintained by Mexico's Ministry of Health. In all health districts in the country, standardized coders obtain information from death certificates. The Ministry of Health centralizes this information after correction, validation, and integration, at the health district level.

SEED has been previously used for mortality follow-up and shown to have a sensitivity for detecting deaths approaching 90%.[14] We performed cross-linkage using a probabilistic record linkage algorithm specifically developed for Mexico by the Public Health Intelligence Unit at the National Institute of Public Health.[15] This procedure achieved a sensitivity of 91% and a positive predictive value of 97% for identification of deaths. This algorithm has been previously used for linkage of CNPSS' reimbursement claims with SEED and has shown to perform well.[16,17] Briefly, the national identification number (CURP for its Spanish acronym), first and two last names, and date of birth were used for cross-linkage. Using the names as the initial blocking variables we identified pairs with high similarity. We compared them using CURP and date of birth to identify those with a high similarity score (≥0.9) and classified pairs as matching, potentially matching, and non-matching records. Matching pairs were retained, potentially matching pairs were reviewed manually, and

non-matching pairs discarded. We obtained the underlying cause of deaths and other causes of death from death certificates and used ICD-10 codes C50.0–C50.9 for breast cancer.

Statistical analysis

The primary outcomes were overall and clinical stage-specific 5-year breast cancer survival. Five-year survival according to age, marginalization, and type of facility (location, funding, and patient volume) were secondary outcomes. We first explored the distribution of clinical stage and calculated 95% confidence intervals (95% CI) according to age, year of treatment initiation, and state where the woman was treated. Women were followed from the date of registration in the FPGC database until death from any cause, or December 2017, whichever happened first. We used the Kaplan–Meier method to calculate overall- and clinical stage-specific survival and corresponding 95% confidence intervals (95% CI). We used the log-rank test to compare survival curves across groups. For survival analyses, we excluded women with missing information on clinical stage and women with stage 0 (*in situ* carcinomas) as we were interested in understanding survival of patients with invasive breast cancer. After peer-review, we conducted a sensitivity analysis that included in the overall 5-year survival estimation women with *in situ* disease. We also calculated overall 5-year survival according to year of treatment initiation (this was only done for the 29,270 patients who initiated treatment between 2007 and 2013 to guarantee 5-year follow-up as participants were administratively censored in December 31, 2017 because of study ending) and state of residence. Because clinical stage at diagnosis is an important predictor of survival and differences in survival may be attributed to the distribution of clinical stage, we also standardized the 5-year survival estimates using the clinical stage distribution observed nationally (in this analysis) and calculated the corresponding 95% CIs. We used SAS (Statistical Analysis Software 9.4, SAS Institute Inc., Cary, NC) for data management and RStudio (Version 1.2.5033, Boston, MA) for data analysis.

Role of the funding source

The authors received no funding for this study.

Results

Median age of study participants was 52 years (interquartile range [IQR] 45, 61) (Table 1). Approximately 25% (14,060/56,847) of patients were younger than 45 years, and 29% (16,605/56,847) older than 60 years. The majority (64%, 36,490/56,847) lived in non-marginalized municipalities. Sixty-five percent (36,731/56,847) were treated when breast cancer was locally advanced or metastatic. While the majority received treatment in the same state where they lived, 22% (12,750/56,847) were treated in a different state. The majority of women received treatment in state-funded hospitals (80%, 45,567/56,847).

Median age, years	52 (interquartile rage, 45–61)	
	n	%
Age categories		
<40	6800/56,847	12.0
40–44	7260/56,847	12.8
45–49	9270/56,847	16.3
50–54	8967/56,847	15.8
55–59	7945/56,847	14.0
60–64	5987/56,847	10.5
65–69	4339/56,847	7.6
70–74	2747/56,847	4.8
75+	3532/56,847	6.2
Municipality of residence		
Marginalized	10,242/56,847	18.0
Not marginalized	36,490/56,847	64.2
Missing[a]	10,115/56,847	17.8
Clinical stage		
In situ	1070/56,847	1.9
Early	16,204/56,847	28.5
Locally advanced	31,347/56,847	55.1
Metastatic	5384/56,847	9.5
Missing[a]	2842/56,847	5.0
Out-of-state treatment	12,750/56,847	22.4
Federal-funded facility	11,280/56,847	19.8
Hospital patient volume		
Low	20,544/56,847	36.1
Medium	15,611/56,847	27.5
High	20,692/56,847	36.4

[a]Values were not recorded in the database.

Table 1: **Characteristics of 56,847 women treated for breast cancer under Seguro Popular between 2007 and 2016 in Mexico.**

The distribution of clinical stage at treatment initiation appears to have remained relatively stable over the 10-year period (Fig. 1). Early-stage disease fluctuated between 26% (602/2305) and 30% (1670/5651). The proportion of cases in this stage was 26% (602/2305; 95% CI 23–30%) for 2007 and 29% (2843/9790; 95% CI 27–31%) for 2016. The proportion of women treated with metastatic disease was 10% (241/2305; 95% CI 7–14%) in 2007 and 9.5% (933/9790; 95% CI 8–10%) in 2016. However, estimates need to be interpreted with care because in 2013 and 2016, we found an increased proportion of women for whom cancer stage was missing (from 2–5% to 11%). Locally-advanced and metastatic disease was more common among women younger than 40 years old (75%, 5065/6800) in contrast with 59% (7704/13,073) among women aged 60–74) (Supplementary Table S1). Clinical stage distribution appeared to differ according to state of residence (Supplementary Table S2). The proportion of women detected in localized stages (*in situ* or early stage) ranged

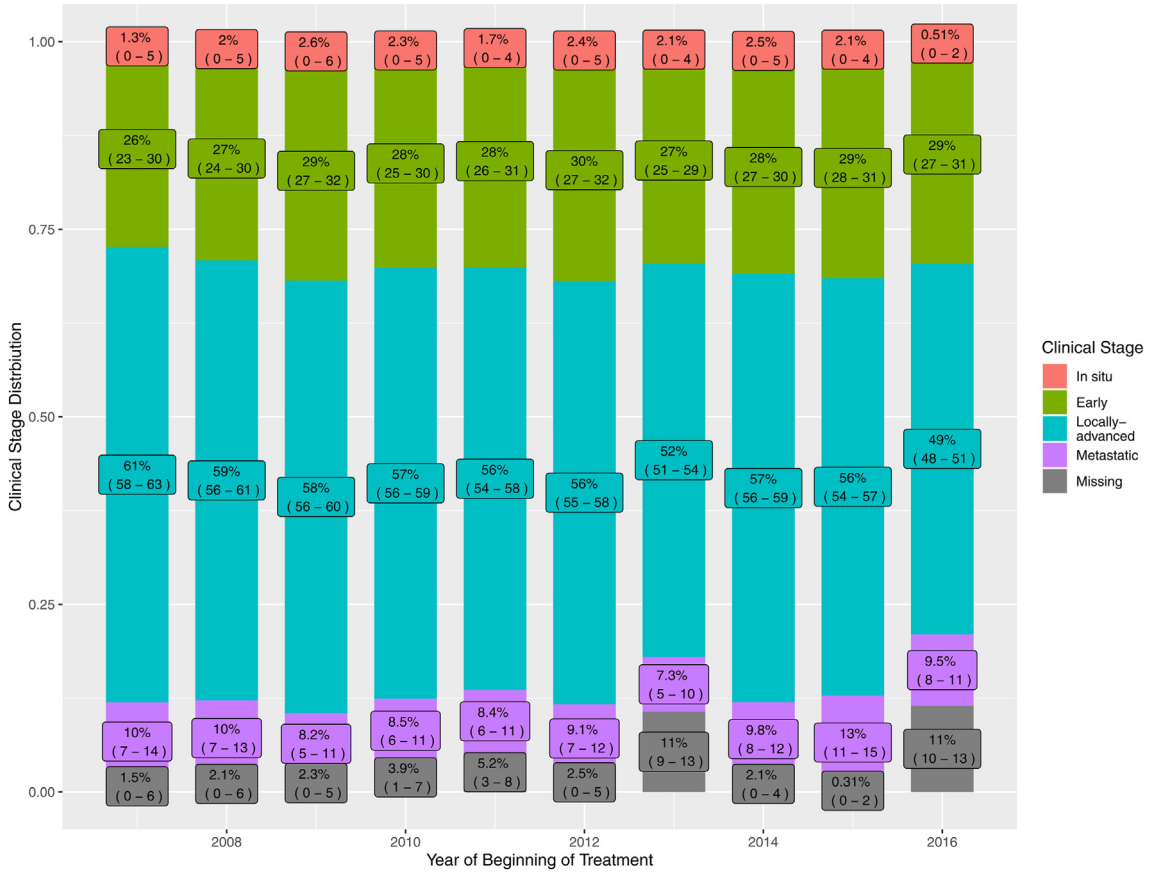
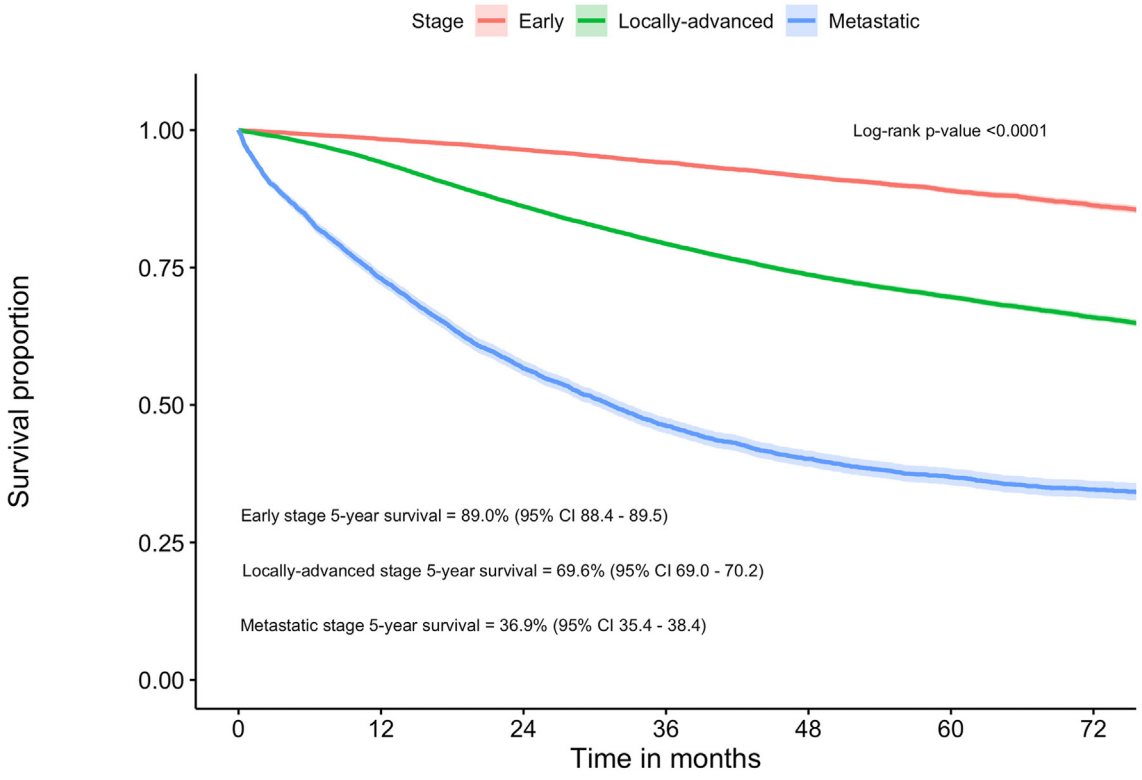


Fig. 1: **Distribution of clinical stage according to year of treatment initiation in 56,847 women treated for breast cancer under Seguro Popular between 2007 and 2016 in Mexico.**

between 18% (61/342) and 45% (135/298) across states. For metastatic disease, this proportion ranged from 5% (69/1363) to 16% (10/64). For example, early disease was observed in 18% (168/939) (95% CI 12–24%) of women from Chiapas and in 34% (259/773) (95% CI 28–39%) in women from Colima.

Median follow-up for the 56,847 participants was 3.5 years (IQR, 2.0, 5.8). We observed 14,110 deaths over the study period (for 81% breast cancer was the underlying cause of death or one of the causes of death). Five-year overall survival was 72.2% (95% CI 71.7, 72.6). Our sensitivity analysis including women with *in situ* carcinomas showed very similar 5-year overall survival (72.7%; 95% CI 72.2, 73.1). For early disease, 5-year overall survival was 89.0% (95% CI 88.4, 89.5). The corresponding estimate for locally advanced disease was 69.6% (95% CI 69.0, 70.2) and for metastatic disease it was 36.9% (95% CI 35.4, 38.4) (Fig. 2). Characteristics of women included in survival analyses as well as those excluded because stage at diagnosis was *in situ* or missing or because of sex (i.e., men) are shown in Supplementary Table S3.

We estimated 5-year survival for seven cohorts defined by year of treatment initiation (2007–2013, n = 29,270). Five-year clinical stage-specific survival remained relatively constant among women who began treatment in this period (Table 2). We found important variation in 5-year survival rates across states where patients received treatment. The state with the lowest survival was Chiapas (55.9%; 95% CI 52.2, 89.8), while the state with the highest survival was Colima (77.2%; 95% CI 73.2, 80.7) (Supplementary Figure S2). For stage-specific 5-year survival, differences across states appeared to be more marked (Supplementary Table S4). The two states with the lowest overall 5-year survival (i.e., Chiapas and Veracruz) had an important proportion of marginalized municipalities (Supplementary Table S5). However, other states with more than 60% marginalized municipalities (i.e., Guerrero and Oaxaca) showed overall 5-year survival above the national average. One-, 2-, 3-, and 4-year stage-specific survival rates are reported in Supplementary Table S6. When we estimated the 5-year survival that would have been observed assuming that the states had the same



Early							
At risk	16,204	15,936	13,202	10,709	8,378	6,404	4,721
Cumulative events	0	268	553	848	1,110	1,322	1,489
Locally-advanced							
At risk	31,347	29,519	23,323	17,959	13,469	10,094	7,435
Cumulative events	0	1,837	4,206	5,915	7,060	7,732	8,214
Metastatic							
At risk	5,384	3,932	2,602	1,628	1,096	798	554
Cumulative events	0	1,456	2,284	2,716	2,902	2,984	3,028

Fig. 2: **Breast cancer 5-year survival by clinical stage in 52,935 women treated for breast cancer under Seguro Popular between 2007 and 2016 in Mexico.** 1070 women with *in situ* disease and 2842 women with missing clinical stage were excluded from this analysis. p-value for the log-rank test <0.0001.

distributions of clinical stage as the national average, we found that the differences in standardized survival estimates became less salient but important heterogeneity remained (Supplementary Table S7 and Supplementary Figure S3). For example, for Chiapas the clinical stage-standardized 5-year survival was 60.1% (95% CI 56.3, 63.9) but it remained the state with the lowest survival.

When we explored stage-specific survival in patient subgroups, we observed that the lowest survival estimates for all disease stages were observed among the youngest (<40 years) and the oldest (≥75) women (Table 3). Patients seeking treatment outside their state of residence appeared to have somewhat higher survival, particularly women with metastatic disease: 46.1% (95% CI 43.2, 49.2) vs. 33.3% (95% CI 31.6, 35.1). Survival

Year	Early	Locally-advanced	Metastatic
2007	89.5 (87.1–92.0)	69.8 (67.4–72.2)	32.8 (27.4–39.3)
2008	88.6 (86.5–90.8)	69.3 (67.2–71.4)	41.6 (36.5–47.4)
2009	89.8 (88.0–91.6)	72.0 (70.1–73.9)	32.5 (27.7–38.1)
2010	89.6 (88.0–91.4)	69.9 (68.1–71.7)	27.9 (23.7–32.8)
2011	89.9 (88.3–91.5)	69.9 (68.2–71.6)	33.3 (29.1–38.2)
2012	91.0 (89.7–92.4)	70.4 (68.8–72.0)	40.3 (36.3–44.8)
2013	87.2 (85.3–89.2)	68.3 (66.6–69.9)	37.7 (33.7–42.2)

We excluded 664 women with *in situ* disease, 1,536 with missing values for clinical stage, and 25,377 women treated in 2014–2016.

Table 2: **Clinical stage-specific breast cancer 5-year survival (95% confidence interval) according to year of treatment initiation (n = 29,270 women).**

appeared to be somewhat higher in women treated in federally funded hospitals relative to those treated in state funded facilities. For metastatic disease, there were better survival rates in high patient volume facilities (41.9%; 95% CI 39.5, 44.4) than in low patient volume hospitals (33.1%; 95% CI 30.8, 35.7).

Discussion

We estimated overall and stage-specific survival for breast cancer for Mexican women without social security health insurance, representing close to 60% of the population. Most women had advanced disease at treatment initiation. The clinical stage at treatment initiation remained relatively stable between 2007 and 2016. And, between 2007 and 2013, no improvement in 5-year breast cancer survival was observed. Stage and survival differed across age groups, states, and type of facility where women received treatment.

Cancer survival is a key indicator of health system performance in the management of cancer.[5] It reflects the capacity of a health system to detect cancer early and to provide timely access to high quality diagnostic tests and treatment.[2] Where population-based cancer

	Clinical stage		
	Early	Locally-advanced	Metastatic
Age			
<40	86.7 (84.6–88.9)	63.8 (62.2–65.5)	31.3 (27.5–35.5)
40–44	90.7 (89.1–92.4)	71.6 (70.1–73.2)	39.3 (35.1–44.0)
45–49	92.1 (90.0–93.4)	72.2 (70.8–73.6)	40.3 (36.5–44.5)
50–54	90.4 (89.0–91.8)	72.1 (70.7–73.6)	36.7 (32.9–40.9)
55–59	90.5 (89.0–91.9)	70.8 (69.2–72.4)	36.4 (32.5–40.7)
60–64	89.3 (87.7–91.0)	72.0 (70.1–73.9)	40.2 (35.7–45.3)
65–69	87.1 (85.1–89.1)	70.3 (68.0–72.6)	37.9 (32.9–43.7)
70–74	85.2 (82.5–88.0)	67.6 (64.8–70.6)	38.8 (32.9–45.9)
≥75	79.5 (76.5–82.6)	59.3 (56.7–61.9)	31.5 (26.5–37.4)
Log-rank test p-value	<0.001	<0.001	0.031
Municipality of residence[a]			
Marginalized	89.7 (88.2–91.1)	70.3 (68.9–71.7)	39.7 (36.0–43.8)
Not marginalized	90.5 (89.8–91.2)	73.5 (72.7–74.2)	39.2 (37.1–41.5)
Log-rank test p-value	0.78	<0.001	0.70
Location of treatment			
In state	88.8 (88.1–89.4)	68.5 (67.8–69.2)	33.3 (31.6–35.1)
Out-of-state	90.1 (88.9–91.3)	73.4 (72.2–74.5)	46.1 (43.2–49.2)
Log-rank test p-value	0.07	<0.001	<0.001
Hospital funding			
Federal	90.3 (89.1–91.5)	73.1 (71.8–74.4)	41.1 (38.2–44.2)
State	88.6 (87.9–89.3)	68.8 (68.1–69.4)	35.5 (33.8–37.3)
Log-rank test p-value	0.01	<0.001	0.02
Hospital patient volume			
Low	89.1 (88.2–90.0)	68.0 (67.1–69.0)	33.1 (30.8–35.7)
Medium	87.7 (86.5–88.9)	67.8 (66.7–69.1)	34.9 (32.0–38.0)
High	89.7 (88.7–90.6)	72.7 (71.7–73.7)	41.9 (39.4–44.4)
Log-rank test p-value	0.01	<0.001	<0.001

Analyses exclude 1070 women with *in situ* disease and 2842 women with missing clinical stage were excluded from this analysis. [a]8,692 women were excluded because information on municipality of residence was unavailable.

Table 3: **Breast cancer 5-year survival (95% confidence interval) according to participant and facility characteristics (n = 52,935).**

registries (PBCRs) are available cancer survival can be accurately measured and used as a policy tool for monitoring and evaluation of cancer care.[18] Where PBCR coverage is low, the use of administrative databases has been shown to provide useful estimations.[19] In Mexico, like in most LMICs, PBCR coverage is low.[20] Until recently, Mexico did not have a PBCR even though more than 200,000 new cancer cases occur every year. The PBCR in southern Mexico that began in 2015 covers slightly less than one million (0.7%) individuals in a country with a population of 135 million. In this context, our study provides a useful example of how the linkage of medical claims data from health insurance systems to mortality data may be efficiently leveraged to provide cancer survival estimates. While these results may not be transportable to women treated for breast cancer in social security systems, we provide survival estimates that can be used to benchmark current and future cancer care programs.

We estimated that between 2007 and 2013, 5-year overall survival for uninsured women with breast cancer in Mexico was 72%. Our estimated survival in Mexico appears to be comparable to other Latin American upper middle-income countries like Chile (76%) and Colombia (72%). Nevertheless, it lags 12 percentage points behind Argentina, Brazil and most high-income countries.[21,22] While our results are only directly generalizable to the uninsured population in Mexico, there are no other reliable breast cancer survival estimates for Mexico for this and for the insured population. The few publications on breast cancer survival in Mexico report survival above 80% but reflect hospital experiences in Mexico City in a national cancer referral center[23] and a private hospital that were financed by *Seguro Popular*[24] and results from two private hospitals in Northern Mexico.[25]

Stage-specific national survival rates (89% for early stage and 36.9% for metastatic stage) were lower than what is observed in high-income countries (early stage 97.4%, metastatic stages 38%), although they are similar in certain high-volume centers.[21] Close to 70% of our study participants initiated treatment with advanced-stage disease (IIB–IV). Our findings are similar to those reported for nine countries in Latin America (n = 15,070) where 64% of patients were diagnosed in stages IIB–IV between the years 2000 and 2016.[26] In contrast, this proportion is less than 40% in high-income countries.[22] Thus, lower survival in Mexico, and other middle-income countries may be in part attributable to a higher proportion of cases treated with advanced disease.

We found that survival differed according to age, geographical location, and characteristics of the facility where the patient received treatment. We observed lower survival rates among the youngest and oldest age groups. Worse outcomes have been reported for both age groups.[27,28] Among younger women, late-stage disease may be the result of more aggressive tumor behavior[29] or delays in appropriate diagnostic work-up.[30] Previous studies in Mexican population have reported that women younger than 40 years are diagnosed at more advanced stages, and have higher proportion of high grade, luminal B, and triple negative tumors.[31] It has also been reported that younger Mexican women face longer time intervals for diagnosis of breast cancer compared to their older counterparts, which has been explained by the lack of cancer suspicion by primary care physicians.[32] As for older patients, late presentation may be the result of insufficient screening, as most country guidelines (including Mexico's) recommend screening up to 70 or 75 years of age, and of delayed diagnosis due to comorbidities and access barriers more often faced by older women.[28] Additionally, elderly women are commonly undertreated which may further hamper their prognosis.[28]

We observed important geographical variations in survival in a setting where women received standardized treatment regimens. The variation was not fully explained by clinical stage at treatment initiation. Also, some states with a high proportion of marginalized municipalities had 5-year survival above the national average. Thus, while living in a marginalized municipality may have impacted timely diagnosis and cancer treatment, access to quality breast cancer treatment and adherence are likely to play an important role in these regional differences. Also, the presence of high-volume centers might be playing a role in the observed geographical variations in survival. Independently of disease stage, survival and quality of care for breast cancer have been reported to be higher in high patient-volume facilities.[33,34] This is consistent with our findings that patients who received care outside of their state of residence at federally funded hospital (which tend to be larger and better funded) and at high-patient volume facilities had higher survival rates. High volume centers are more likely to have the institutional infrastructure and the multidisciplinary healthcare personnel required to deliver high quality complex multidisciplinary breast cancer treatment. Also, there may be a limited general capacity for cancer care in certain states. The three lower ranking states in breast cancer survival are among the states with the lowest survival for acute lymphoblastic leukemia in children.[17]

Even though *Seguro Popular* was eliminated in 2019, treatment for breast cancer among the population not covered by social security continues to be offered at the same public federal and state hospitals and is financed through a revised funding mechanism. Our results offer a baseline analysis of breast cancer outcomes (clinical stage distribution and survival) that can facilitate evaluation of the impact of recent changes in Mexico's health system.

The lack of changes in the distribution of clinical stage at treatment initiation and survival has important implications. While Mexico expanded access to standard

multimodal breast cancer treatment for patients without social security,[35] the policy did not change cancer stage at time of patient registration or breast cancer survival over a ten-year period. This is likely a consequence of having focused efforts solely on enhancing access to specific medical services without implementation of mechanisms to assure early diagnosis and quality of care of the services provided. High-quality care involves thorough clinical assessment, accurate diagnosis, appropriate and timely treatment and referrals, and the ability to follow the patient and adjust the treatment course as needed.[36]

The advanced presentation of most breast cancer cases in Mexico is a consequence of prolonged times in diagnostic confirmation.[20] Delays between the patients' symptom discovery and treatment are associated with more advanced disease stage at diagnosis and poorer survival.[37–39] We previously reported that even in large cancer referral centers in Mexico City 85% of breast cancer patients are first seen by clinicians when symptoms are already present and time to diagnostic confirmation may be as prolonged as five months.[32,40] These diagnostic delays are likely the results of misdiagnosis at the primary care level, access barriers (including costs) that affect prompt referrals and diagnosis, and long appointment waiting times in public facilities.[32,41]

Appropriate access to diagnostics (including primary care) is central and fundamental to quality health care and should be incorporated into universal health coverage packages.[42] Diagnostic mammography, breast ultrasound, and biopsy tests were not covered by *Seguro Popular*, even though diagnostic confirmation was a prerequisite for financing treatment. Thus, out-of-pocket expenditure to complete the diagnostic workup was a likely contributor to delays.

Strengths and limitations of this study

The main strengths of our study are the use of a nationwide comprehensive reimbursement dataset representing a large proportion of breast cancer cases occurring in Mexico between 2007 and 2016, availability of information on 10 of the 13 years that the voluntary insurance scheme was in place and the use of a robust data-linkage to mortality data procedure.

Our study has some limitations. The analyses included only population without social security, therefore our results do not provide information on women that received care in one of the social security systems or the private sector. However, our study provides information on a large proportion breast cancer cases treated in Mexico during the study period (i.e., 57% by 2016).[43] Additionally, since we used administrative data, which was not designed for research, we lack data on the specific treatment that the patients received, as well as patient adherence and completion of treatment plans. Our analysis assumes participants completed their treatment in the same facility where the first reimbursement claim was filed. As the number of accredited facilities increased and the fee-for-service reimbursement mechanism became more granular, patients could potentially receive treatment in more than one facility. However, this is likely to be infrequent because there were only a very limited number of facilities per state. Relative to studies based on retrospective medical record reviews or prospective data collection, our analysis did not include clinical information that would be useful to characterize with more detail this group of patients (e.g., molecular subtypes) and evaluate secondary outcomes like relapse or progression of the disease. Nevertheless, the advantage of this administrative data which was collected in order to reimburse hospitals for patient treatment is that there was a natural incentive to collect data for all cases.

Conclusions

We found breast cancer survival rates in Mexico to be comparable to other upper middle-income countries in Latin America. Nevertheless, in the ten-year period analyzed, despite treatment financing no improvement in breast cancer survival was observed. This could be due to the lack of changes in advanced stage presentation, which is likely the consequence of access barriers and quality issues for timely cancer diagnosis confirmation. These findings could serve as an example for other countries when designing universal health coverage packages: it shows how increased access to cancer treatment, although necessary, is not enough in and of itself. To improve cancer outcomes, increased access to treatment needs to be coupled with improvements in early diagnoses, so that patients may benefit from receiving treatment in early stages, when it is more likely to be effective. Additionally, this study demonstrates how the linkage of medical claims data from health insurance systems to mortality data may be efficiently leveraged to provide cancer survival estimates in the absence of population-based cancer registries.

Contributors

KUS, JEH, PCG, AM, and ML were involved in conceptualization of this study. ABJ, RHG, and SZM were involved in the formal data analysis. KUS, ABJ, RHG, SZM, and ML were involved in the methods development. All authors were involved in data interpretation. KUS and ML wrote the original draft of the paper. ABJ produced the manuscript figures and tables. All authors were involved in reviewing and editing drafts of the paper. ABJ, RHG, and ML accessed and verified the raw data used in this study. All authors had full access to data in the study and had final responsibility for the decision to submit for publication.

Data sharing statement

This study was based on administrative data from Mexico's National Commission for Social Protection in Health (CNPSS for its acronym in Spanish). We do not own these data and hence are not permitted to share them in the original form. However, data can be made available on request via email to the corresponding author.

Declaration of interests

Paula Cabrera-Galeana reported receiving consulting fees from Pfizer, Novartis, and Roche, and payment or honoraria from Roche, Lilly, and Pfizer. Other authors report no potential conflict of interest.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.lana.2023.100541.

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