Introduction

In Mexico, as in other developing countries, breast cancer (BC) incidence and mortality has been increasing, and represents the main cause of cancer death in Mexican women since 2006. Among the factors that contribute to the current burden of BC in Mexico are the low coverage of screening mammograms, barriers to timely diagnosis,
limited access to standard treatment, and suboptimal quality of healthcare services, which are predominant in the population with public healthcare coverage.\textsuperscript{2,3}

The Mexican healthcare system comprises two sectors, the private (which includes medical services covered by insurance companies in private offices, clinics and hospitals) and the public sector (which includes medical services covered by governmental policies in specific government financed hospitals).\textsuperscript{4} The public sector covers approximately 95\% of the Mexican population, while the private sector is responsible for the remaining 5\%.\textsuperscript{5} Seguro Popular was created in 2003 as a health reform to address the low healthcare budget and unfair distribution of medical services in Mexico and to provide medical services for the uninsured population.\textsuperscript{4,6–8} Until December 2019, 40.8\% of the Mexican population was covered by Seguro Popular.\textsuperscript{9,10} Management of the most common neoplasms (cervical, breast, testicular, prostate, and non-Hodgkin lymphoma), bone marrow transplantation, and cancer in children, was covered free of charge for 51.4 million Mexicans by Seguro Popular.\textsuperscript{8,10}

Since an important proportion of the Mexican population has public healthcare coverage and previous studies in high-income countries have shown that lack of medical insurance is a leading driver for disparities in BC detection and mortality,\textsuperscript{11–17} it is relevant to study whether the previously described association occurs in limited resource settings. Thus, we hypothesized that patients with public healthcare coverage in Mexico would have worse outcomes than women with private medical insurance. The generation of this local data is crucial for developing strategies to identify gaps in BC diagnosis and treatment. Therefore, the main objective of this study is to compare the sociodemographic, diagnostic, clinical, and treatment-related characteristics and outcomes of patients with BC in two hospitals in Mexico with different medical coverage.

**Methods**

**Study design**

A retrospective cohort study was conducted to compare patients with BC in two hospitals in Mexico according to their type of healthcare coverage. Study procedures were reviewed and approved by the TecSalud’s Institutional Review Board.

**Setting**

Since the incorporation of BC to Seguro Popular, BC diagnosis and treatment were provided to women, free of charge, through accredited hospitals.\textsuperscript{18} A fixed budget for individual patients was calculated according to clinical stage at diagnosis, which resulted in access to some high-priced therapies and tests, (an additional budget was only allocated for trastuzumab), certain treatment modalities such as breast reconstruction, and supportive services.\textsuperscript{19,20} Most of Seguro Popular’s accredited centers were public hospitals; however, some private healthcare centers, including Hospital San Jose Tec de Monterrey (HSJ), were also certified as Seguro Popular BC centers.\textsuperscript{21}

**TecSalud**

The Breast Cancer Center of TecSalud, active at two hospitals, HSJ and Hospital Zambrano Hellion (HZH), offers comprehensive BC management by a multidisciplinary team of BC specialists, in accordance with international guidelines.

TecSalud is a unique instance where patients with both coverages, Seguro Popular and private medical insurance, were treated. Since 2010, HSJ was accredited by Seguro Popular for the diagnosis and treatment of BC, and more than 1,800 women were treated at HSJ under the coverage of Seguro Popular.\textsuperscript{18} Meanwhile, more than 1,300 patients with private medical insurance have received treatment at HZH since 2014. Noteworthy, genetic and genomic testing of patients with Seguro Popular is not routinely covered but was possible through two research protocols in TecSalud.

**Participants**

The pathology registry of the TecSalud hospitals, including HSJ and HZH, was reviewed to identify patients diagnosed with BC between August 1st, 2014 and July 31st 2017. Subsequently, medical records were screened to identify patients who received cancer treatment at TecSalud hospitals. Patients’ records were thoroughly reviewed to collect type of healthcare coverage, as well as sociodemographic, clinical, pathological, diagnostic, treatment, and outcome characteristics. Those patients whose complete information was unavailable for all the variables included in this study or received BC treatment other than in TecSalud hospitals were excluded.

**Variables**

The patients included in this study were categorized according to their type of healthcare coverage as “private healthcare coverage” and “public healthcare coverage” (those covered by Seguro Popular). The following variables were retrieved from medical records: demographic characteristics (age, marital status, and occupation), clinical (menopausal status, height, weight, and body mass index (BMI)), diagnostic (onset of symptoms, date of diagnosis, method of diagnosis, and clinical stage at diagnosis), pathological (histological subtype and molecular subtype), treatment (start date of treatment, initial treatment, surgical treatment, systemic treatment and radiotherapy), and outcomes (recurrence, mortality, recurrence-free survival and overall survival). Diagnosis interval was calculated from the date of
first symptom/mammogram to the date of histopathological diagnosis, treatment interval from the date of histopathological diagnosis to the treatment starting date, and total interval from the date of first symptom/mammogram to the treatment starting date.22

Statistical methods

Descriptive statistics were used to analyze demographic, clinical, diagnosis, pathological, treatment, and outcomes characteristics. To compare patients with public and private coverage, chi-square test was used for categorical variables and Student’s t-test or Mann–Whitney U-test for quantitative variables according to their distribution. We further analyzed the association between healthcare coverage and treatment (initial systemic therapy, overall chemotherapy, and radiotherapy) given the stage of the disease (early, locally advanced, and metastatic) using a Mantel–Haenszel test. A value of \( p < 0.05 \) was considered statistically significant. Additionally, Cramer’s V was calculated for nominal variables to evaluate the strength of association.

An exploratory survival analysis was performed using Kaplan–Meier curves to compare recurrence-free and overall survival in patients with public and private healthcare coverage. The curves were statistically compared using the log-rank test. Sub-analyses were performed by clinical stage and BC subtype. The software used for data analysis was SPSS (Statistical Package for the Social Sciences).

Table 1. Sociodemographic and clinical characteristics.

|                         | Total n = 282 (100%) | Private n = 73 (100%) | Public n = 209 (100%) | p     | Cramer’s V |
|-------------------------|----------------------|-----------------------|-----------------------|-------|-----------|
| Age at diagnosis (years)| 52.4 ± 12.4          | 52.3 ± 13             | 52.5 ± 12.2           | 0.90  | –         |
| Marital status          |                      |                       |                       |       |           |
| • Partnered             | 190                  | 67.4%                 | 56                    | 76.7% | 134       | 64.1% | 0.048 | 0.12 |
| • Unpartnered           | 92                   | 32.6%                 | 17                    | 23.3% | 75        | 35.9% |       |      |
| Employment status       |                      |                       |                       |       |           |
| • Homemaker             | 210                  | 74.5%                 | 42                    | 57.5% | 168       | 80.4% | 0.001 | 0.23 |
| • Unemployed            | 3                    | 1.1%                  | 1                     | 1.4%  | 2         | 1%    |       |      |
| • Employed              | 69                   | 24.5%                 | 30                    | 41.1% | 39        | 18.7% |       |      |
| Weight (kg)             | 71 ± 14.5            | 68.4 ± 1.6            | 73.2 ± 14.7           | 0.01  | –         |
| Height (m)              | 1.59 ± 0.06          | 1.61 ± 0.06           | 1.58 ± 0.06           | <0.001| –         |
| BMI (kg/m²)             | 28.6 ± 5.9           | 26.3 ± 5.2            | 29.4 ± 6.0            | 0.001 | –         |
| • Underweight           | 4                    | 1.4%                  | 1                     | 1.4%  | 3         | 1.4%  | 0.01  | 0.23 |
| • Normal                | 77                   | 27.3%                 | 28                    | 38.4% | 49        | 23.4% |       |      |
| • Overweight            | 96                   | 34%                   | 30                    | 41.1% | 66        | 31.6% |       |      |
| • Obesity I             | 69                   | 24.5%                 | 10                    | 13.7% | 59        | 28.2% |       |      |
| • Obesity II            | 21                   | 7.4%                  | 3                     | 4.1%  | 18        | 8.6%  |       |      |
| • Obesity III           | 15                   | 5.3%                  | 1                     | 1.4%  | 14        | 6.7%  |       |      |
| Menopausal status       |                      |                       |                       |       |           |
| • Postmenopausal        | 153                  | 54.3%                 | 37                    | 50.7% | 116       | 55.5% | 0.45  | 0.42 |
| • Premenopausal         | 129                  | 45.7%                 | 36                    | 49.3% | 93        | 44.5% |       |      |

BMI: Body mass index.

Results

A total of 320 patients were both diagnosed and treated for BC at TecSalud hospitals; 38 patients were excluded because medical records were lacking complete information. Therefore, the analysis of this study includes a total of 282 patients with BC; 73 (25.9%) women had private healthcare coverage; and 209 (74.1%) had public healthcare coverage by Seguro Popular.

Mean age at diagnosis was 52.4 (±12.4) years, with no difference between groups. More women with private healthcare coverage were partnered (married or in domestic partnership) (76.7% vs 64.1%, \( p = 0.048 \)) and employed (41.1% vs 18.7%, \( p = 0.001 \)) compared to women with public healthcare coverage. Women with public healthcare coverage had a higher BMI than women with private healthcare coverage (29.4 vs 26.3 kg/m², \( p = 0.001 \)), and a higher proportion of women with public healthcare coverage were overweight and obese (75.1% vs 60.3%, \( p = 0.01 \)). Regarding menopausal status, 54.3% of the patients included were postmenopausal, with no difference between groups. Sociodemographic and clinical characteristics are included in Table 1.
respectively), while no difference was found in treatment interval (0.70 vs 0.60 months, p = 0.20). Overall, infiltrating ductal carcinoma (81.6%) was the most frequent histopathological subtype, and hormone receptor (HR) positive (HR+) HER2 negative (HER2–) BC was the most prevalent subtype (67.7%), with no difference between groups. Complete characteristics related to BC diagnosis are found in Table 2.

More patients with public healthcare coverage underwent initial systemic treatment (41.1% vs 17.8%, p < 0.001), overall chemotherapy (79.4% vs 43.8%, p < 0.001), and adjuvant radiotherapy (68.9% vs 53.4%, p = 0.017). However, given stage at diagnosis, the association between healthcare coverage and treatment was only maintained for overall chemotherapy (Mantel–Haenszel p < 0.001). Similarly, more women with public medical coverage underwent mastectomy (70.1% vs 54.9%, p = 0.20). On the contrary, more women with private medical coverage underwent breast reconstruction (66.7% vs 8.4%, p < 0.001). Regarding primary systemic treatment, 44% of the women included received neoadjuvant chemotherapy, and of these, 26.1% presented a complete pathological response, without differences between groups. More women with public healthcare coverage received chemotherapy regimens including anthracyclines (95.2% vs 84.4%, p = 0.043), while more patients with private healthcare coverage received dose-dense chemotherapy (15.6% vs 3.6%, p = 0.023). No differences were found in the use of other chemotherapy agents. Complete details of BC treatment are described in Table 3.

Regarding the specific treatment for BC patients with HR+ and HER2+ tumors, women in both groups received hormonal therapy and HER2-directed therapy alike. Patients with private healthcare coverage with HER2+ disease received more dual HER2 blockade (33.3% vs 2.7%, p = 0.002) than patients with public healthcare coverage. The characteristics of endocrine and anti-HER2 therapies are shown in Table 4.

As for additional testing, only 10.6% of the total population underwent a genetic test to detect germline mutations related to hereditary BC and more women with private medical coverage had such testing performed (17.8% vs 8.1%, p = 0.021). No differences were found in the prevalence of mutations between groups and four results were pending at the time of this analysis. Finally, in terms of performing genomic tests for predictive and/or prognostic value, more women with private healthcare coverage had genomic testing done (39.7% vs 5.3%, p < 0.001).

The median follow-up was 36.6 (25.8–45.1) months. Overall, rate of recurrence was 9.9%, 4.3% corresponding to patients with private insurance and 11.9% to patients with public insurance (p = 0.14). Overall mortality rate was 6.7%, 2.7% in patients with private medical coverage and 8.1% in those with public medical coverage (p = 0.11). Due to the low prevalence of events (recurrence or death), free-recurrence and overall survival medians are not reported, instead, cumulative proportions of patients without events were calculated at the median follow-up time.

Recurrence-free survival (90.1%) was not statistically different between groups (p = 0.259). The 3-year recurrence-free survival was 92.6% for patients with private healthcare coverage and 87.8% for those with public healthcare coverage (p = 0.14). Subgroup analysis by stage and subtype showed numerical differences but no statistically significant differences. Trends suggesting worse recurrence-free were observed in patients with public healthcare at 36 months follow-up in stage III (85.7% vs 67.3%, p = 0.25) and triple negative disease (83.3% vs 74.5%, p = 0.58). Recurrence-free survival Kaplan–Meier curves are shown in Figure 1.

Overall survival (93.3%) was also not found to be statistically different between groups (p = 0.180). The 3-year

| Table 2. Diagnosis characteristics. |
|-----------------------------------|
|                                   |
| Total n = 282 (100%) Privaten = 73 (100%) Public n = 209 (100%) | p | Cramer’s V |
|-----------------------------------|
| Method of detection               |
| • Self-detected                   | 208 | 73.8% | 35 | 47.9% | 173 | 82.8% | <0.001 | 0.35 |
| • Mammography                     | 74  | 26.2% | 38 | 52.1% | 36  | 17.2% |
| Diagnosis interval (months)       | 1.6 | (0.4–5.3) | 0.5 | (0.2–1.5) | 2.2 | (0.7–7.0) | <0.001 | – |
| Treatment interval (months)       | 0.6 | (0.4–1.1) | 0.6 | (0.4–1.02) | 0.7 | (0.4–0.7) | 0.20 | – |
| Total interval (months)           | 2.6 | (1.2–7.3) | 1.2 | (0.7–2.2) | 3.2 | (1.6–8.9) | <0.001 | – |
| Clinical stage at diagnosis       |
| • 0                               | 14  | 5%    | 6  | 8.2%  | 8   | 3.8%  |
| • I                               | 46  | 16.3% | 19 | 26%   | 27  | 12.9% |
| • II                              | 144 | 51.1% | 35 | 47.9% | 109 | 52.2% |
| • III                             | 68  | 24.1% | 10 | 13.7% | 58  | 27.8% |
| • IV                              | 10  | 3.5%  | 3  | 4.1%  | 7   | 3.3%  |
overall survival was 96.3% for patients with private healthcare coverage and 91.3% for patients with public healthcare coverage (p = 0.18). Subgroup analysis by stage and subtype showed numerical differences but no statistically significant differences. Trends suggesting worse overall survival were observed in patients with public healthcare at 36 months follow-up in stage III (100% vs 84.6%, p = 0.22) and triple negative disease (100% vs 74.1%, p = 0.18). Overall survival Kaplan–Meier curves are shown in Figure 2.

**Discussion**

This is the first study in Mexico to compare the characteristics and outcomes of patients with BC according to healthcare coverage, and only the second in Latin
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Furthermore, it is the first of its kind in Latin America to compare women with both types of healthcare coverages treated within the same hospital system.

Although the inclusion of BC within Seguro Popular provided treatment coverage to many Mexican women who would have not previously received it, this study...
Martinez-Cannon et al. found that women with public healthcare coverage still present longer diagnostic and total intervals. Estimated diagnosis (2.2 months) and total (3.2 months) intervals in patients with public medical coverage in this study may have contributed to more advanced stage at diagnosis; however, these delays were shorter than those reported in

Figure 2. Overall survival: (a) Overall survival at 36 months follow-up was 96.3% for patients with private healthcare coverage and 91.3% for those with public healthcare coverage. (b) Overall survival in early clinical stage (0–II). (c) Overall survival in advanced clinical stage (III) at 36 months follow-up was 100% for patients with private medical coverage and 84.6% for those with public medical coverage. (d) Overall survival in HER2+ disease. (e) Overall survival in HR+ disease. (f) Overall survival in TN disease at 36 months follow-up was 100% for patients with private healthcare coverage and 74.1% for those with public healthcare coverage.
another Mexican study, where the diagnosis and total intervals were 5 and 7 months, respectively. The reasons for these timeframe differences are not known, though, the study conducted by Unger-Saldaña et al. was carried out in four different public healthcare institutions in Mexico City, including two hospitals covered by Seguro Popular and two hospitals by the Instituto Mexicano del Seguro Social (Mexican Institute of Social Security); therefore, patient referral and waiting times may vary within the different healthcare systems. Also, geographical, population-size, and healthcare system capacity differences might influence variations in intervals.

Furthermore, patients with public medical coverage had more advanced disease at diagnosis than those with private healthcare coverage, as described in other previous studies. This could be explained by the high percentage of BC diagnoses made by self-detection (82.8% vs 47.9%, p < 0.001), rather than by screening mammography in patients with public healthcare coverage. A previous Mexican study identified that advanced BC stages at diagnosis are associated with diagnosis delay, which in turn is influenced by patients' lack of BC awareness (dismissing symptoms as “not worrisome”), limited social network (the longer a patient conceals her symptoms from others, the longer she delays medical care), financial difficulties in seeking care (unable to justify taking medical leave from their jobs), as well as perception of medical errors in diagnostic impressions of the first doctors consulted. Strategies to reduce diagnosis delays in Mexico and other low- and middle-income countries should not rely on population-based mammography, but on addressing the previously described barriers. Therefore, Mexican healthcare policy to promote early diagnosis and to reduce diagnosis delay should focus on guaranteeing access to the basic cancer diagnosis resources, including prioritized, high-quality, and diagnostic mammography and clear referral systems for symptomatic patients.

Furthermore, advanced stage at diagnosis is treated with trimodal therapy, including systemic therapy, surgery, and radiotherapy. In this study, the higher prevalence of advanced disease could have contributed to the greater number of patients with public coverage who received initial systemic treatment, overall chemotherapy, and adjuvant radiotherapy, as was also observed in the studies by Liedke et al. and Y Zhang et al. Regarding surgical treatment, it was found that patients with public healthcare coverage underwent more radical mastectomies and less breast reconstruction compared to those with private healthcare coverage, as also previously reported. Regarding systemic treatment, patients with HER2+ disease with public healthcare coverage received less dual HER2 blockade compared to those with private healthcare coverage, as Seguro Popular previously covered treatment only with trastuzumab.

Regarding survival rates according to healthcare coverage, previous studies have reported an association between worse outcomes and public medical insurance. However, in our study, patients with public healthcare coverage did not have worse recurrence-free and overall survival than patients with private healthcare coverage. It could be argued that the absence of differences in survival between patients with private and public healthcare coverage may have been influenced by the fact that patients with Seguro Popular had access to the main treatment modalities as patients with private healthcare coverage at TecSalud; therefore, all patients were treated in a similar fashion, by the same group of healthcare professionals with equal infrastructure, regardless of medical coverage. Furthermore, the healthcare model of the Breast Cancer Center at both TecSalud hospitals is delivered through a multidisciplinary team of BC specialists, as multidisciplinary care has been associated with improved BC outcomes in previous studies.

Two reports in Mexico have demonstrated improved BC outcomes since its incorporation to Seguro Popular’s coverage. A study conducted at the Hospital Universitario “Dr. Jose Eleuterio Gonzalez,” in Monterrey, Mexico, found an improvement in recurrence-free and overall survival when comparing patients diagnosed before and after BC inclusion within the coverage of Seguro Popular. Likewise, a study conducted at the Instituto Nacional de Nutricion y Ciencias Medicas Salvador Zubiran, in Mexico City, found a higher recurrence rate in patients treated prior to the coverage of Seguro Popular than in patients covered by Seguro Popular.

Noteworthy, trends suggesting worse outcomes were observed in patients with public healthcare in stage III and triple negative disease. Although the reasons of these differences are unclear, it might be related to limitations to key therapeutic strategies in the public system, as the use of pertuzumab in addition to trastuzumab, ovarian function suppression agents, dose-dense chemotherapy with granulocyte-colony stimulating factors, CDK4/6 inhibitors and immunotherapy.

It is important to comment on the fact that a large proportion (75.1%) of the patients with Seguro Popular were overweight and obese. Prior studies analyzing the relationship between socioeconomic status and obesity have found a positive association between low socioeconomic status and obesity, although the causes of this relationship are unknown. Furthermore, obesity has been described as a risk factor for developing BC and as a prognostic factor associated with worse survival and recurrence.

In this study, more than a third of the patients with Seguro Popular had no partner compared to less than a quarter of patients with private medical coverage. It has been reported that BC patients who do not have a partner (single, widows, and divorced) have worse outcomes than those with a partner (married or in domestic partnership). It is suspected that the benefits of having a partner are probably related to a better structure and functioning of the patient’s social support network.
Among the limitations of this study is its retrospective nature, which may have impaired data collection. Also, average monthly income of the patients included is not known; hence, the type of medical healthcare coverage does not necessarily reflect socioeconomic status. In addition, short follow-up and small sample size might have had some effect in the lack of difference in outcomes. Another limitation is that selection bias cannot be ruled out since data on excluded patients due to missing information on medical records were not recollected and analyzed. The most important strength of this study is that patients of both groups were diagnosed and treated within the same hospital system, so the healthcare professionals and facilities were the same for all patients and the differences found are due to extrinsic factors.

In conclusion, the findings of this study show that patients with public healthcare coverage present with more self-detected tumors and advanced disease at the time of diagnosis than those with private medical coverage. Strategies to promote preventive medicine, the use of diagnostic mammography, and early diagnosis of BC in Mexican women with public healthcare coverage need to be developed and implemented. Similarly, more research is needed to identify barriers that delay BC detection and treatment initiation in patients with public healthcare coverage so as to develop targeted interventions to shorten these timeframes.

The second major contribution of this study is the observation of similar outcomes between patients with private and public healthcare coverage, which are likely explained by the access to the main treatment modalities by Seguro Popular and high quality care by an experienced group of physicians. However, trends suggesting worse survival for patients with public medical coverage with stage III triple negative disease should encourage close follow-up and targeted interventions.

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