Improving Outcomes for Women with Triple-Negative Breast Cancer in Latin America – An Extended Analysis

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## Foreword

Breast cancer is the most common cancer type in women in Latin America. Triple-negative breast cancer (TNBC) is the most challenging subtype of breast cancer to treat. It is more aggressive than most other subtypes and has the worst prognosis. TNBC disproportionately affects younger women, often in their reproductive and working years. This not only compounds the medical complexity of the disease but also underscores its profound societal and economic implications. In contrast to other subtypes, therapeutic innovations in the medical treatment of TNBC have been absent for many years. However, the recent introduction of immunotherapy and targeted therapy might be the beginning of a new era for TNBC patients. Despite this progress, the disparity in treatment access persists, as many Latin American countries still rely predominantly on chemotherapy due to the unavailability of these advanced therapies.

This present report is an extension of the IHE Report 2023:6 "Improving outcomes for women with triple-negative breast cancer in Latin America". The updated report adds three additional countries to the analysis (Dominican Republic, Panama, and Peru). It describes characteristics of TNBC patients and the disease and economic burden to society in eight countries in Latin America: Argentina, Brazil, Chile, Colombia, Dominican Republic, Mexico, Panama, and Peru. It analyzes challenges that patients face along key stages - detection, diagnostics, and treatment - of the care pathway and discusses the societal impact of improved TNBC care. High-level recommendations for improvement of TNBC care are also provided.

Lund, March 2024

Peter Lindgren Managing Director, IHE





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### Summary

In Latin America, breast cancer is a major and growing public health concern, accounting for 29% of all new cancer cases and 17% of all cancer deaths among women. One of the most aggressive and challenging subtypes of breast cancer is triple-negative breast cancer (TNBC), accounting for 13-21% of all breast cancer cases in the region.

### Challenges in early detection of TNBC

TNBC is often diagnosed at a late stage when the tumor has already started to spread beyond the breast and when survival chances are low. In Peru, the 5-year survival rates for TNBC range from 92% in cases diagnosed early in stage I to 5% in cases diagnosed when the tumor has already metastasized in stage IV. Affecting slightly younger women than other breast cancer subtypes, TNBC tumors also tend to grow faster than other subtypes. This makes early detection - through self-detection and screening - particularly crucial. Current challenges for early detection of TNBC in Latin America include:

- Low awareness of early signs of breast cancer and fear of diagnosis among women
- Lack of primary care physicians leading to long waiting times for women to receive a breast cancer diagnosis
- Lack of training of primary care staff in identifying breast cancer symptoms
- Absence of nationwide organized population-based screening programs, such as in Mexico
- Shortage of mammography machines and lack of quality control
- Inadequate information-sharing on screening services and long waiting lists to get a screening appointment
- Accessibility barriers to screening for women living in rural areas
- Low perceived quality of screening services in the public sector

### Challenges in diagnostics and treatment of TNBC

TNBC is the most difficult-to-treat subtype of breast cancer irrespective of stage at diagnosis. TNBC tumors lack the hormone receptors and HER2 receptors that are targeted by hormonal therapy and HER2-targeted therapies, respectively. For this reason, until recently, chemotherapy was the only medical treatment option for TNBC patients. Despite the use of chemotherapy, TNBC was characterized by a higher tumor recurrence rate and a poorer prognosis compared with all other subtypes. For instance, the 5-year survival rate for breast cancer cases diagnosed in stage I-III is 76% for TNBC and 88% for non-TNBC cases in Chile. Since 2018, new medical treatment options for TNBC have emerged. They include immunotherapy and targeted therapy (for patients with *BRCA* mutations).

Timely breast diagnostics and appropriate treatment are vital to increase the survival prospect of TNBC patients. Current challenges in diagnostics and treatment of TNBC in Latin America include:



- Poor coordination between providers of diagnostic services and treatment, resulting in long delays to receive treatment in the public sector
- Shortages of pathologists, oncologists, and radiologists, and insufficient education and training
- Limited access to multidisciplinary teams (MDTs)
- Lack of diagnostic infrastructure
- Lack of comprehensive biomarker testing
- Outdated national clinical guidelines
- Late approval of innovative treatments by regulatory agencies compared with the US FDA
- Lack of availability of new treatments in the public sector
- Disruptions in the supply of reimbursed medicines
- Use of counterfeit medicines
- Slow adoption of new treatment approaches in clinical practice

### Societal effects of improved TNBC care

Improving the quality of care - from early detection to diagnostics and treatment - of TNBC patients can positively affect the survival of patients and their quality of life. This would help to reduce the future disease burden of TNBC.

Improvements in the care of TNBC also have wider implications for society, including effects on health systems, work life, family life and the need for informal care, and the economy. For instance, improved early detection would have the following effects:

- Treatment costs would decrease, because the per-patient costs of breast cancer diagnosed in stage I (US\$ 13,179) are less than half that of stage IV (US\$ 28,910) according to a pooled study of Latin American countries.
- More women would be able to continue to work during their initial treatment or resume work after it, because the symptom burden is lower in early stages than in late stages of breast cancer.
- The increased number of women able to resume work and survive TNBC would reduce indirect costs (productivity loss to the economy). Indirect costs of breast cancer are considerable and almost equally as large as treatment costs, according to a study from Mexico, because breast cancer affects many women of working age.
- An improved health status would also ease the need for informal care by family members.



### Areas of improvement in TNBC care

There are ample opportunities to improve the quality of TNBC care. This report has pinpointed the following three broad areas and recommendations to improve the care of TNBC patients in Latin America. The recommendations are directed towards various stakeholders in each area.

Raise health literacy to facilitate early detection	Ensure optimal care delivery	Consider adoption of innovation in clinical practice	
<ul> <li>✓ Improve breast cancer prevention</li> <li>✓ Raise awareness of breast cancer symptoms</li> <li>✓ Enhance involvement of primary care in early detection</li> <li>✓ Personalize risk assessment through <i>BRCA</i> genetic testing</li> <li>✓ Promote participation in screening programs</li> </ul>	<ul> <li>Address the underfunding and fragmentation of health care systems</li> <li>Overhaul national breast screening programs</li> <li>Establish clear care pathways</li> <li>Assure high quality of breast cancer imaging</li> <li>Ensure a swift and complete pathological assessment before treatment start</li> <li>Recruit and train pathologists, oncologists, and radiologists</li> <li>Consolidate MDTs in main institutions</li> <li>Ensure timely availability and utilization of prescribed medicines</li> </ul>	<ul> <li>✓ Expand access to comprehensive biomarker testing</li> <li>✓ Enhance regulatory efficiency</li> <li>✓ Take steps to expand access to appropriate medicines in the public sector</li> <li>✓ Update local clinical guidelines</li> <li>✓ Update care pathways and provide training to clinical staff</li> </ul>	
	Key stakeholders		
<ul> <li>Citizens and patients</li> <li>Patient advocacy groups</li> <li>Health care professionals (primary care)</li> <li>Media</li> <li>Ministry of Health</li> <li>Social security institutions</li> </ul>	<ul> <li>Health care professionals (breast cancer specialists)</li> <li>Hospitals and diagnostic centers</li> <li>Ministry of Health</li> <li>Social security institutions</li> </ul>	<ul> <li>Medical associations</li> <li>Hospitals and diagnostic centers</li> <li>Health care professionals</li> <li>Ministry of Health</li> <li>Social security institutions</li> </ul>	

## List of abbreviations

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ARS	Health insurance companies
ASCO	American Society of Clinical Oncology
BMI	Body mass index
BRCA 1/2	Breast cancer gene 1/2
CDK	Cyclin-dependent kinase
COFEPRIS	The Federal Commission for Protection against Health Risks
CSS	Panamanian Social Security Fund
EMA	European Medicines Agency
ENSPA	National Health Survey of Panama
ER	Estrogen receptor
ESMO	European Society for Medical Oncology
ESTRO	European Society for Radiotherapy and Oncology
FDA	Food and Drug Administration in the United States
GBCI	Global Breast Cancer Initiative
GDP	Gross domestic product
HER2	Human epidermal growth factor receptor 2
HIC	High-income countries
HRQoL	Health-related quality of life
IAEA	International Atomic Energy Agency
IARC	International Agency for Research on Cancer
IMSS	Mexican Social Security Institute
INCAN	National Cancer Institute
INCART	Rosa Emilia Sánchez Pérez de Tavares National Cancer Institute
INEN	National Institute of Neoplastic Diseases
ION	National Oncology Institute
IREN	Regional Institute of Neoplastic Diseases
KPI	Key performance indicator
MDT	Multidisciplinary team
MINSA	Ministry of Health
PBS	Health Benefits Plan

### Country abbreviations

- ARG = Argentina
- BRA = Brazil
- CHL = Chile
- COL = Colombia
- DOM = Dominican Republic
- MEX = Mexico
- PAN = Panama
- PER = Peru

## 1. Introduction

This report focuses on triple-negative breast cancer (TNBC) in Latin America. It describes patient characteristics (chapter 2), the disease and economic burden to society (chapter 3), current challenges in patient access to TNBC care (chapter 4), and the societal impact of improved TNBC care (chapter 5). It also provides a comprehensive set of recommendations to a wide group of stakeholders for future improvements (chapter 6). Country cards that summarize the main findings and recommendations for each country are provided in the Annex.

A more detailed medical description of the current global standard of care for TNBC was previously published in IHE Report 2023:2 (1). This report focused mainly on high-income countries in Europe and Northern America. A separate report - IHE Report 2023:3 - covering five countries and territories in Asia-Pacific (Australia, Hong Kong, South Korea, Taiwan, and Thailand) was also published (2).

### Geographic scope

The main geographic focus is eight countries in Latin America: Argentina, Brazil, Chile, Colombia, Dominican Republic, Mexico, Panama, and Peru.

#### Methodology

This report employs a pragmatic review of publicly available literature to bring together evidence on the landscape of breast cancer and TNBC across the included countries. The main content draws on the structure of the breast cancer care pathway delineated in the World Health Organization (WHO) Global Breast Cancer Initiative (GBCI) (see chapter 4). To ensure a thorough review of the literature, sources in English, Spanish, and Portuguese were consulted. These included scientific articles and grey literature such as reports, governmental publications, and policy documents.

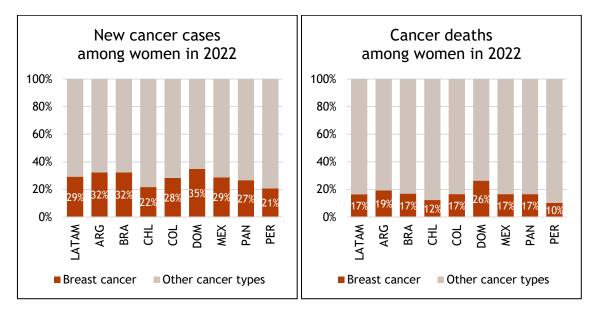
Feedback received during public presentations of the original IHE Report 2023:6 at the 2<sup>nd</sup> Simposio Oncolatino in Mexico and the 20<sup>th</sup> Latin America Health and Science Journalism Program in Brazil were also taken into account in this extended report.



## 2. Breast cancer and TNBC

### 2.1 Breast cancer

Breast cancer occurs in every country of the world in women<sup>1</sup> at any age after puberty, but with increasing likelihood later in life (4). Breast cancer is the most common type of cancer among women in Latin America and the Caribbean (5). In 2022, an estimated 219,684 new breast cancer cases were diagnosed in the region and 59,701 women died from the disease. In Latin America, breast cancer is responsible for 29% of all new cancer cases and 17% of all cancer deaths in women; see Figure 1 (5). The estimated average risk for a woman to get breast cancer (before the age of 85) is close to 8%. In countries such as Argentina and Brazil, this risk is even higher (10% and 9%, respectively) and close to rates in high-income countries (HIC) in Europe and Northern America.



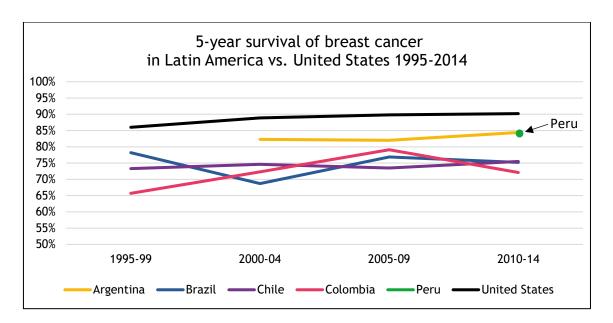
## Figure 1: Proportion of new breast cancer cases and deaths among women in Latin America in 2022.

Notes: Cancer was defined as all types excluding non-melanoma skin cancer. Latin America includes all countries across the region and the Caribbean. Source: Estimates by IARC (5).

In HIC, survival rates in breast cancer have started to improve substantially since the 1980s with the introduction of hormonal therapies and the establishment of screening programs that increased early detection (4). Nowadays, 80-90% of women with breast cancer in HIC are still alive five years after diagnosis, while countries in Latin America are lagging behind with rates of 72-84%; see Figure 2. In addition, the gap in survival rates between Latin American countries and HIC did not seem to have changed in recent decades; see Figure 2.

<sup>&</sup>lt;sup>1</sup> Men can also get breast cancer, but it is rare. Only about 1 out of every 100 breast cancer cases diagnosed in the United States is found in men (3). This report focuses on women with breast cancer.





## Figure 2: 5-year age-standardized relative survival of breast cancer in Latin American countries and the United States in 1995-2014.

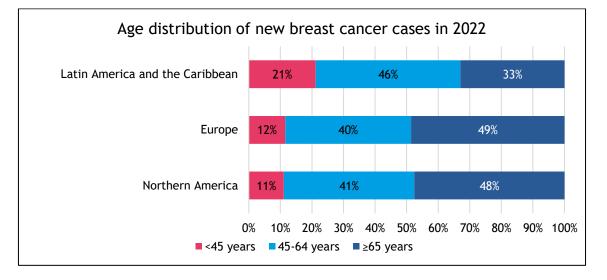
Notes: Data was gathered from regional registries that covered in 1995-99 and 2000-14 the following national population: 9.2% in Argentina, 5.7% and 7.7% in Brazil, 5.5% and 13.8% in Chile, 6.9% and 9.0% in Colombia, respectively. Data for 2010-2014 covered 24.4% of Peru with a 5-year survival rate of 84%. Historic data for Mexico was unavailable, but research from 2010-2015 estimated the absolute 5-year survival rate to be 81% in a single hospital in Mexico City (n=197) (6). Source: CONCORD (7, 8).

Lower survival rates of breast cancer patients in Latin America than in HIC have previously been attributed to several factors (9):

- Inadequate investment in health care and unequal access to health care among populations with different insurance plans have resulted in varying survival rates. Studies from Brazil and Mexico show that breast cancer patients in advanced stages with public health insurance face a lower survival rate compared with those with private health insurance (10, 11).
- Low rate of early breast cancer detection, leading to 30-40% of cases being diagnosed at an advanced stage compared with only 10% in the European Union (9). In countries like Mexico and Peru, around half of detected breast cancer cases are in advanced stages (stage III and IV) (12, 13). In the Dominican Republic this number increases to 58% (14). Women treated in the public sector in Mexico, Argentina, Brazil, and Chile have a higher likelihood of being diagnosed at a late stage, compared to women treated in the private sector, as indicated in section 4.2.
- Limited access to innovative cancer medicines such as targeted treatments (9). However, at least basic diagnostic testing for hormone receptors and human epidermal growth factor receptor 2 (HER2) is comparatively well-established and carried out in most but not all patients (9).

Breast cancer is more common in younger women in Latin America than in Europe and Northern America; see **Figure** 3. In Mexico, for instance, the median age at diagnosis is 51 years, which is more than ten years younger than the median age in Europe and the United States (15). **Figure** 3 shows that one fifth of all breast cancer cases are diagnosed in women below the age of 45 and two thirds in women below the age of 65. The younger age distribution in Latin

America has negative consequences for the social and economic impact of breast cancer. Many women below the age of 45 might have dependent children to take care of. Women of working age who are forced to be on sick leave due to treatment-related morbidity or who die prematurely represent a productivity loss for the economy.



**Figure 3: Age distribution of new breast cancer cases in 2022 by world region.** Source: Estimates by IARC (5).

### 2.2 What is TNBC?

Breast cancer is composed of several distinct subtypes that differ in their biological characteristics. They are typically classified into four types based on the tumor's expression of estrogen receptor (ER), progesterone receptor (PR), and HER2 (16, 17); see Table 1. The most common subtype is luminal A, which is hormone-receptor positive (i.e., ER and PR positive) and HER2-negative. TNBC is defined as a subtype of breast cancer in which neither ER, PR, nor HER2 are overexpressed (18). The word "negative" in TNBC thus simply refers to the lack of any of the three receptors.

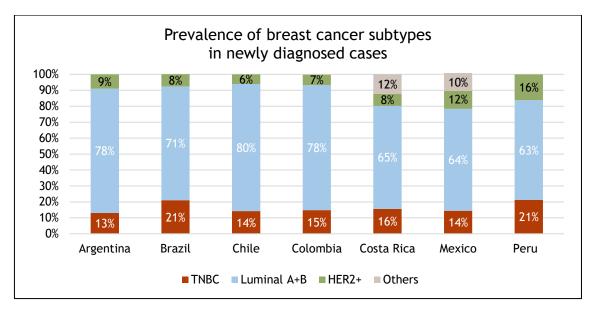
Subtype	Expression of receptors		
Luminal A	ER-positive, PR-positive, HER2-negative		
Luminal B	ER-positive, PR-any-level, HER2-positive		
HER2+	ER-negative, PR-negative, HER2-positive		
TNBC	ER-negative, PR-negative, HER2-negative		

### Table 1: Breast cancer subtypes

The treatment of TNBC varies based on the stage at diagnosis and typically includes a mix of surgery, radiation therapy, and systemic therapy (i.e., cancer medicines). Systemic therapy options depend on tumor characteristics and differ therefore between breast cancer subtypes. Owing to the lack of expression of the three main receptors in breast cancer, TNBC tumors do not respond to hormonal therapies or HER2-targeted therapies as other subtypes of breast cancer (19). Systemic therapy options for TNBC up until very recently had been restrained to chemotherapy (20), which kills/damages fast-growing tumor cells but also fast-growing healthy cells in the body. However, since 2018, new systemic therapies have emerged with the advent of immunotherapies and *BRCA*-targeted treatments; see section 4.4.



TNBC accounts for around 10-20% of all newly diagnosed breast cancer cases globally (21). Figure 4 shows that the prevalence of TNBC is between 13% and 21% in the selected Latin American countries. These numbers are, however, not based on population-based cancer registries, but rather on studies with comparatively small populations. They should therefore be interpreted with caution (22). A recent study from Chile found a lower proportion of only 11%, which is similar to US-resident Hispanics (23). Nonetheless, several studies have pointed out that TNBC seems to be more frequent in Latin America than in other regions of the world (24).



# Figure 4: Prevalence of breast cancer subtypes in newly diagnosed cases in Latin America. Notes: Data for Chile correspond to the average of new breast cancer diagnosis in women $\leq$ 40 years and $\geq$ 70 years, for this reason it might not be representative. Data for Argentina and Colombia were gathered from studies with small populations, n=174 and n=377, respectively. Data for Costa Rica was used as a proxy for the Dominican Republic and Panama as country-specific data was not available. Source: (22, 25-29).

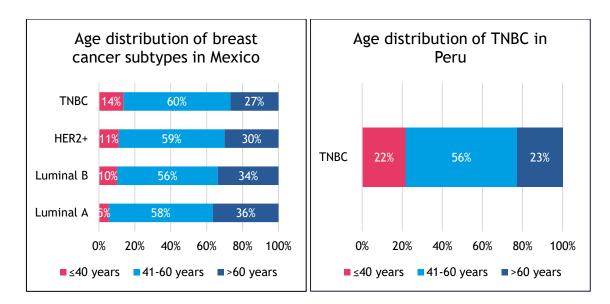
A key feature of TNBC is the younger age at diagnosis compared with other breast cancer subtypes; see Figure 5 for an example from Mexico. The median age at diagnosis is generally below 50 years (30, 31). In a couple of studies in Peru the median age of diagnosis of TNBC has been shown to be 48-49 years (32, 33). In contrast, other study for Peru has estimated the median age of onset for breast cancer overall (encompassing all subtypes) to be higher at 51.3 years (34).

Part 2 of Figure 5 illustrates that, within a study of 2,007 participants, 22% of the patients were below the age of 40. A study from Chile involving 5,806 breast cancer patients found that 16% of TNBC patients were under the age of 40, whereas in the non-TNBC group, this percentage was lower, with only 10% being younger than 40 years (23). In addition, the median age of TNBC patients at diagnosis in Chile was 55.2 years compared with 57.2 years for non-TNBC patients (23).

Young women with breast cancer may face consequences that affect them disproportionally throughout their lives, such as fertility issues linked to treatment with chemotherapy, premature menopause, a high risk of bone density loss, poor mental health, lower quality of life, job loss, and long-term unemployment (35-41).



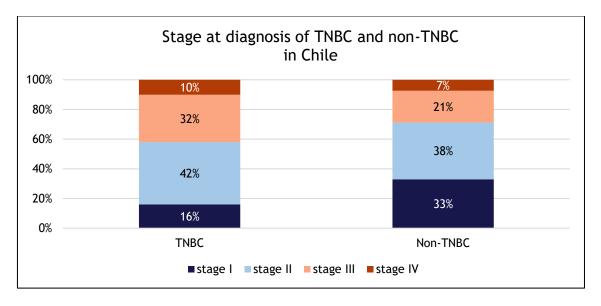




## Figure 5: Age distribution of breast cancer subtypes in Mexico and age distribution of TNBC in Peru.

Notes: For Mexico, patients were diagnosed from January 2011 to December 2014 in two hospitals (n=1,502) of the Mexican Social Security Institute (IMSS). For Peru, the medical records were from the Instituto Nacional de Enfermedades Neoplasicas (INEN) from 2000 to 2014 (n=2,007). Source: (27, 32).

TNBC tumors tend to grow faster than other breast cancer subtypes (42), and they are therefore more likely to be diagnosed at a late stage when the tumor has started to metastasize (i.e., spread to other parts of the body) (43). Figure 6 presents data from a Chilean study that encompassed patients from both the private and public sectors (23). Notably, a substantially greater proportion of TNBC patients are diagnosed late with stage III and IV [42%] than breast cancer patients with other subtypes (28%).



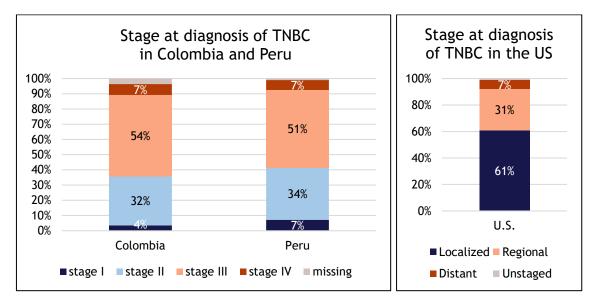
### Figure 6: Stage distribution of TNBC and non-TNBC in Chile.

Notes: n=5,806 breast cancer patients in a public and a private hospital in Santiago. Source: (23).

The stage at which TNBC is diagnosed significantly influences patient survival. Generally, a later diagnosis in the progression of the disease correlates with a poorer prognosis (refer to section 3.2 for more details). In Latin America, TNBC, as well as breast cancer overall, tend to



be diagnosed at more advanced stages compared with HICs. For example, in Colombia and Peru, only about 36% and 41% of TNBC cases, respectively, are detected at an early stage (stages I and II), as shown in Figure 7. In contrast, in the United States, 61% of TNBC cases are diagnosed at a localized stage, which encompasses stage I and some cases of stage II.

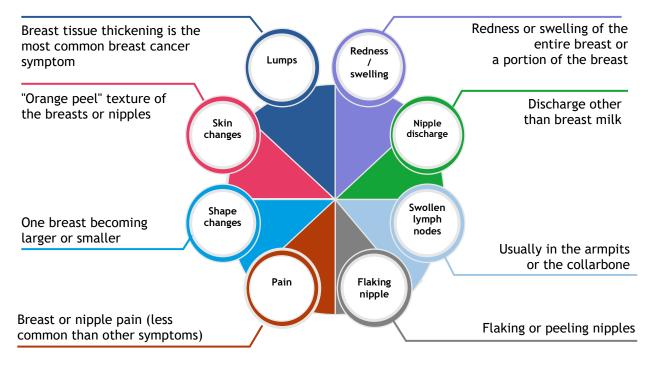


### Figure 7: Stage at diagnosis of TNBC in Colombia, Peru, and the United States.

Notes: Data for Colombia come from a very small sample, n=28. Source: (25, 32, 44, 45).

### 2.3 Signs and symptoms of TNBC

Signs and symptoms of TNBC generally resemble those of other breast cancer subtypes. The most common symptom is a lump or an area of thickened tissue in one of the breasts. Other common symptoms are shown in Figure 8.



### Figure 8: Common signs and symptoms of TNBC.

Source: (46).





### 2.4 Risk factors of TNBC

Many potential risk factors for developing breast cancer have been identified with varying levels of supporting evidence. However, not all of these risk factors have been linked to TNBC. In general, risk factors can be divided into non-modifiable risk factors (see Table 2) and modifiable risk factors (see Table 3) (4).

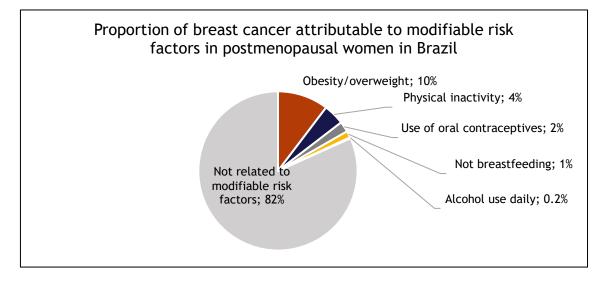
Risk factor	Global / US description	Specifics for Latin America
Age	In the US, the median age for breast cancer diagnosis is around 62 years (47). Risk of developing breast cancer increases with age (48). This is also true for TNBC, but TNBC is more common in younger women than other subtypes (see section 2.2). In the US around 25% of all TNBC cases are diagnosed in women under 50 years, compared with 19% among all breast cancer cases (49).	The mean age of breast cancer diagnosis is lower in Latin American than in the US and Europe, which can be partly attributed to the region's generally younger population demographic. A recent study from Chile found the median age of TNBC patients at diagnosis to be 55.0 years, younger than the median age of non-TNBC patients (57.2 years of age)(23). A study from Peru found the median age at TNBC diagnosis to be 49 years (32).
Family history (Heredity)	Approximately 5-10% of all breast cancers have a hereditary background (50). The most common cause of hereditary breast cancer is an inherited mutation in the <i>BRCA</i> 1 or <i>BRCA</i> 2 gene (50). About 50 out of 100 women with <i>BRCA</i> 1/2 mutations will develop breast cancer by the time they turn 70 years, compared with only 7 out of 100 women in the United States (51). Women with <i>BRCA</i> 1/2 have a particularly high risk of developing TNBC.	The prevalence of <i>BRCA</i> 1/2 mutations in Latin America is not well understood yet, as performing these tests is expensive and most of the countries do not offer genetic testing nor genetic counselling. However, a recent large-scale study showed that these mutations were found in 26% of breast cancer patients in Brazil, 17% in Mexico, 13% in Peru and 9% in Colombia (52). A study from Chile found that TNBC patients were more likely to have inherited genetic mutations than the group with non- TNBC breast cancer (23).
Ethnicity	Black and Hispanic women are at an increased risk of developing TNBC compared with Caucasian women but reasons for this are unclear (53, 54). In the United States, black women are nearly three times more likely than Caucasian women to be diagnosed with TNBC (55).	Brazil has the largest population of African descendants (approximately 50%), followed by Panama and the Dominican Republic with almost 9%, Colombia 7%, Peru 4%, Mexico 1% and Chile and Argentina 0.1-0.4% (56). The prevalence of TNBC in Brazil is higher in the north and northeast regions were more women with African ancestry live (28).
Breast density	Women with a greater breast density (i.e., a greater amount of fibrous and glandular tissues in their breasts) are at a higher risk of developing breast cancer (57). The link between breast density and developing TNBC is stronger in premenopausal women than in postmenopausal women (55).	A study in the United States found that Hispanic women had a higher breast density than African American and Caucasian women (58).

### Table 2: Non-modifiable risk factors in TNBC

According to the WHO, up to 30% of all breast cancer cases are theoretically preventable as they are caused by modifiable risk factors (4). A study from Brazil estimated that around 17% of breast cancer cases in postmenopausal women were attributable to modifiable risk factors



(59); see Figure 9. The largest modifiable risk factor was obesity/overweight, which was attributable to 10% of all breast cancer cases, followed by physical inactivity (4% of all breast cancer cases). Similarly, a study for Chile estimated that around 23% of all breast cancer cases in women were attributable to modifiable risk factors, most of which were related to obesity/overweight and physical inactivity (60).



## Figure 9: Proportion of breast cancer attributable to modifiable risk factors in postmenopausal women in Brazil.

Source: (59).

Risk factor	General description	Specifics for Latin America	
Obesity and overweight	Obesity has been linked with a higher likelihood of developing TNBC (61). For breast cancer overall, the link seems to be stronger in postmenopausal women than in premenopausal women (62).	Obesity rates in Latin America are comparatively high. Chile and Mexico are the countries in the OECD with the highest rates of female obesity (over 30%) (63). Figure 10 shows how female obesity rates have been continuously increasing in all countries since 1975.	
Physical inactivity	A sedentary lifestyle is a risk factor for all breast cancer subtypes, but it appears that the link between physical inactivity and TNBC is stronger (64).	In Latin America, almost half of all women (42%) are physically inactive (63). In 2019, a National Health Survey estimated that 65% of women in Panama were physically inactive (65). A similar proportion has been found in national surveys for women in Peru (66%) (66). Other countries with a high prevalence of female physical inactivity are Brazil (53%), Colombia (48%) and Argentina (45%); see Figure 11.	
Not breastfeeding	Women who never breastfed their babies have a higher risk to get breast cancer in general, and this association has also been established for TNBC (67).	Research indicates that the Dominican Republic has low breastfeeding rates. While on average 30% of infants under 6 months are exclusively breastfed in Latin America, in the Dominican Republic, the rate is only 4% (68).	
No child births	Some studies suggest that having children is associated with a lower risk of hormone-positive breast cancers but a higher risk of TNBC (69). These studies also indicate that the risk of TNBC increases with the number of births, yet the	No studies found on this particular risk factor specific to Latin America.	

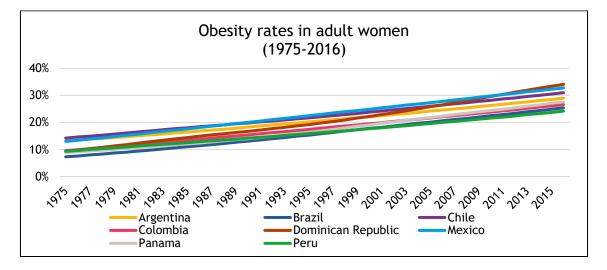
#### Table 3: Modifiable risk factors in TNBC





biological	mechanisms	for	this
association	n are unclear.		

Notes: Alcohol consumption (70), cigarette smoking (71), hormonal replacement therapy to treat menopausal symptoms (72), and use of oral contraceptives (73) have previously been founded to have some (modest) impact on the risk to get breast cancer, but no conclusive links to TNBC have been identified (74, 75).



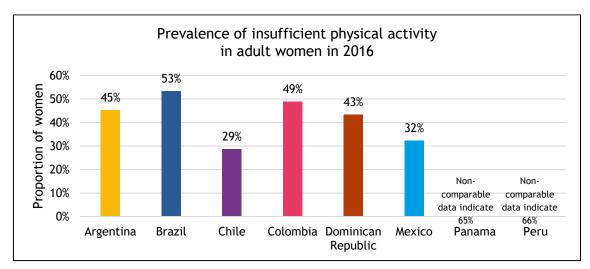


Figure 10: Prevalence of obesity in adult women in Latin America, 1975-2016.

Notes: Obesity is defined as BMI  $\geq$  30. Age group  $\geq$  18 years. Source: WHO (76).

## Figure 11: Prevalence of insufficient physical activity in adult women in Latin America, 2016.

Notes: Age group  $\geq$  18 years. The estimates are derived from a self-reported physical activity questionnaire. To be considered sufficiently active, participants must meet the WHO guidelines for adults, which recommend at least 150 minutes of moderate-intensity exercise or 75 minutes of vigorous-intensity exercise weekly (63). Comparable data specific to Panama and Peru was not available. However, findings from the ENSPA in Panama in 2019 and a population-based survey in Peru with data from 2017-2018 estimated the numbers in the graph (65, 66). Source: OECD (63).

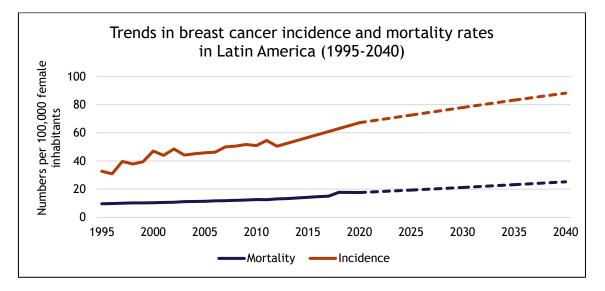


## 3. Disease and economic burden of TNBC

### 3.1 Incidence and mortality

The annual numbers of newly diagnosed cancer cases (i.e., incidence) and cancer deaths (i.e., mortality) are important indicators to measure the disease burden of a specific cancer type in a country. In Latin America, there is some information available on annual breast cancer incidence in many countries, often coming from cancer registries that cover some region(s) of a country; see also section 4.1. However, information on the annual incidence of TNBC is absent in all countries, as this would require routinely measuring the current standard set of molecular markers (e.g., ER, PR, HER2); see section 2.2 for the best available national estimates of the proportion of TNBC from small studies. In contrast, information on the annual breast cancer deaths is readily available from cause-of-death registries in Latin America, yet no information is available for TNBC deaths.

Overall, the estimated incidence rate of breast cancer in Latin America increased from 33 cases per 100,000 women in 1995 to 70 cases per 100,000 women in 2022; see Figure 12. This corresponded to a 113% increase over the whole period. During the same period, the estimated breast cancer mortality rate increased by 83%, from 10 to 18 cases per 100,000 women. The lower relative increase in mortality compared with incidence is a sign of progress in breast cancer care over this period.



## Figure 12: Estimated trends in breast cancer incidence and mortality crude rates per 100,000 female inhabitants in Latin America, 1995-2040.

Notes: The numbers for Latin America are the population-weighted averages of Argentina, Brazil, Chile, Colombia, Dominican Republic, Mexico, Panama, and Peru. Numbers between 2020 and 2040 are predictions based on unchanged age-specific risks to get and die from breast cancer. Source: (77-86).

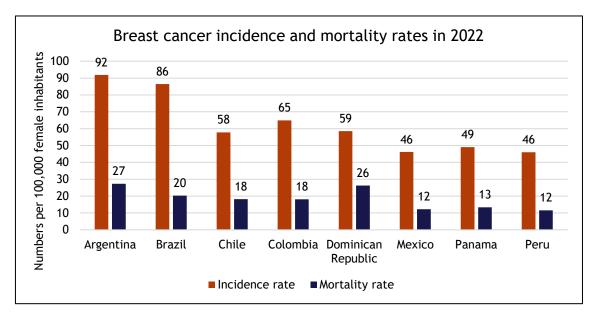
In Latin America, the incidence of breast cancer is predicted to continue increasing. Figure 12 shows predicted increases until 2040 stemming from demographic changes, in particular population aging<sup>2</sup>. If unfavorable developments in risk factors such as obesity (see section 2.4) continue to increase, this will add to the number of new cancer cases shown in Figure 12.

<sup>&</sup>lt;sup>2</sup> The actual increase in TNBC might be slightly lower because the median age at diagnosis of TNBC is lower than the median age at diagnosis of all breast cancer cases (see section 2.2). The effect of





Figure 13 shows breast cancer incidence and mortality rates in individual Latin American countries in 2022. The country with the highest incidence was Argentina, with an estimated 92 cases per 100,000 women. In contrast, Peru had the lowest incidence rate, with 46 cases per 100,000 women. These two countries also had the highest (shared with Mexico) and lowest mortality rates of 27 and 12 deaths per 100,000 women, respectively.



## Figure 13: Breast cancer incidence and mortality crude rates per 100,000 female inhabitants in 2022.

Source: Estimates by IARC (5).

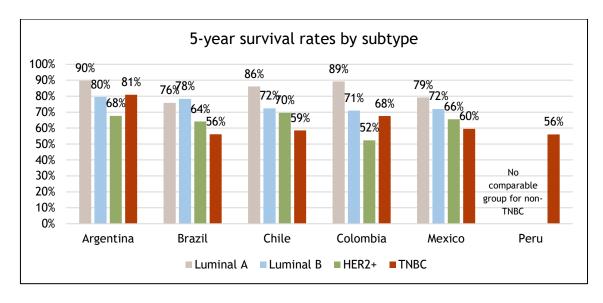
### 3.2 Survival

Survival is a key measure of the disease burden of a cancer type for the individual patient. It measures the likelihood of being alive X years after diagnosis. In the absence of nationwide high-quality cancer registries in Latin American countries, data on survival of patients with TNBC and other breast cancer subtypes are scarce.

Figure 14 summarizes a collection of 5-year survival data points from different research studies for each country. The studies had varying data periods, sample sizes, and clinical features of the included patients, thus limiting comparability. Nonetheless, TNBC patients had the lowest 5-year survival of all breast cancer subtypes at around 60% in Brazil, Chile, and Mexico, which mirrors the survival pattern observed in HIC. In Argentina and Colombia, the survival rate of TNBC patients was higher than that of HER2-positive cancer patients and similar to that of luminal B breast cancer patients.

population aging might thus lead to a somewhat less pronounced increase in TNBC compared with other subtypes.



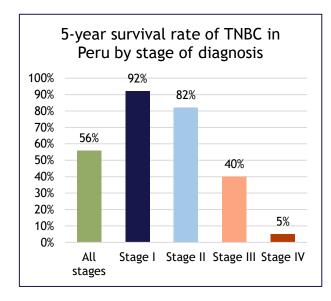


#### Figure 14: 5-year survival rates by breast cancer subtype in Latin America.

Notes: Argentina relative survival in 1998-2017 (n=1,024), Brazil absolute survival in 2001-2006 for stage III patients only (n=454), Chile absolute survival in 1997-2013 for women aged  $\geq$ 70 (n=366), Colombia absolute survival in 2007-2016 (n=4,059), Mexico absolute survival in 2006-2014 (n=880), Peru absolute survival in 2000-2014 (n=2007). No data was available for the other subtypes. Sources: (28, 32, 87-90).

A contributing factor to the comparatively low survival rate for TNBC is its tendency to recur (i.e., come back) after initial treatment (91). While almost 40% of non-metastatic TNBC patients diagnosed in 2004-2012 in Canada experienced recurrence, fewer than 10% of luminal A patients did (92). A study from Chile of breast cancer patients diagnosed in 2010-2021 also found that TNBC patients exhibited a significantly higher risk for early recurrence compared with non-TNBC patients (23).

The stage at which cancer is diagnosed greatly influences the likelihood of survival. The earlier the diagnosis, the better the prognosis. Figure 15 provides an illustration of this pattern in Peru, showing how stage I TNBC patients had a 5-year overall survival rate of 92%, whereas stage III and stage IV TNBC patients had a 40% and 5% 5-year overall survival rate, respectively (32). This is a cause of concern in Latin America, as a significant number of breast cancer diagnoses are made at advanced stages, as noted in section 4.2.



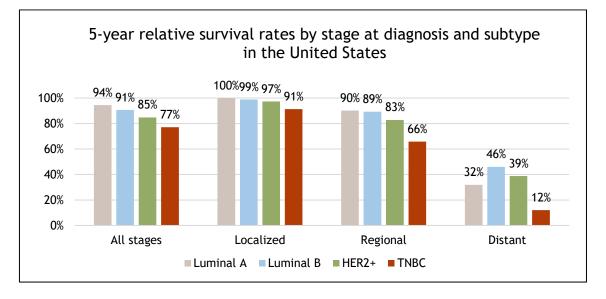
## Figure 15: 5-year overall survival rates of TNBC in Peru by stage of diagnosis.

Notes: The study population was 2,007 newly diagnosed TNBC patients at INEN from 2000 to 2014. Source: (32).

Data from population-based registries, like the SEER in the United States, confirm this pattern of decreasing survival odds with later stage at diagnosis across all breast cancer subtypes. They also show how the survival rates for TNBC at each stage are lower than for other subtypes. Figure 16 shows that when the tumor is still localized at diagnosis, the 5-year relative survival rates of all breast cancer



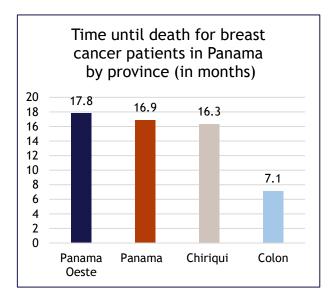
subtypes are close to 100% except for TNBC, which is 91% in the United States. When the tumor has metastasized, the survival rate drops to 12% for TNBC and 32-46% for other subtypes. A study from Chile of breast cancer patients diagnosed in 2010-2021 found that TNBC patients diagnosed in stage I-III had a 5-year overall survival rate of 76%, lower than the 88% in non-TNBC patients; for TNBC patients diagnosed in stage IV the survival rate was 5% compared with 31% in non-TNBC patients (23).



# Figure 16: 5-year relative survival rates by stage at diagnosis and breast cancer subtype in the United States (diagnosis period 2012-2018).

Source: SEER (93).

Another important consideration is that not all women in a specific Latin American country experience the same survival rates. Many women might encounter additional challenges, as is discussed further in chapter 4. As an example of regional differences within a country, Figure 17 highlights disparities across provinces in Panama, where the median survival time for breast cancer patients (with dates of both diagnosis and death between 2012 and 2016) in the province of Panama Oeste is more than twice as long as in Colon.



## Figure 17: Time until death for breast cancer patients by province in Panama.

Notes: Only breast cancer patients with registered diagnosis date and death date between 2012 and 2016 at the National Cancer Registry (RNC) and National Oncology Institute (ION) with evaluable survival data (n=337 out of 4,134) were included. \* The inclusion criteria limit the sample to women diagnosed with advanced/metastatic breast cancer. No separate data for the remaining smaller provinces were included. Source: (94).







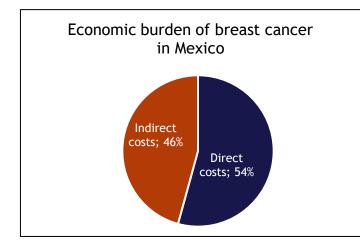
### 3.3 Economic burden

The burden of TNBC on society can also be measured in monetary terms. The costs of TNBC are defined here more broadly than in everyday use. Generally, three types of costs can be distinguished (95); see Table 4.

Direct costs	These are costs of disease-related resource consumption. They include both public and private expenditures for services within the health care system, such as diagnostic procedures, surgeries, radiation therapy, and medicines. Expenditures for social support services outside of the health care system are also direct costs. Expenditures by patients for travelling to receive treatment are also direct costs.	
Indirect costs	These are costs of patients' productivity loss arising from the inability to word due to the disease. They consist of the temporary or permanent inability to word in the formal labor market (called morbidity) and from premature death (called mortality) of working-age people.	
Informal care costs	These are the costs representing the value of the time spent by family members and friends to provide unpaid care, such as transportation to a health care facility and assistance with household chores at home.	

#### Table 4: Components of the economic burden of cancer

Comprehensive analyses of the economic burden of breast cancer and TNBC in Latin America are scarce. Figure 18 shows results from a study for Mexico that estimated both direct costs and indirect costs, with the overall per-patient cost reaching \$49,065 USD per year (96). Direct costs and indirect costs were almost equally large. The high contribution of indirect costs was partly explained by the low age at breast cancer diagnosis, affecting many working-age patients.

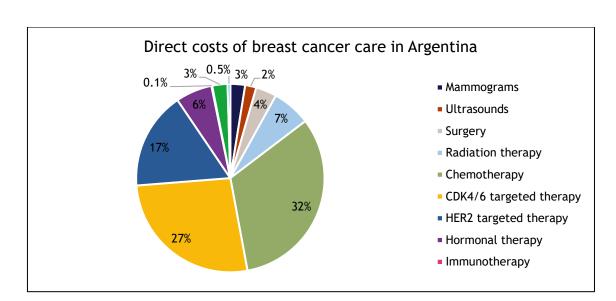


#### Figure 18: Economic burden of breast cancer patients in public health institutions in Mexico in 2014.

Notes: Direct costs include medical costs for diagnosis and treatment as well as funeral costs. Indirect costs include productivity loss from being sick and from premature mortality. Source: (96).

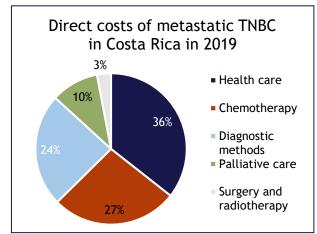
The direct medical costs of breast cancer are composed of the costs of different services received along the patient's journey. Figure 19 shows the distribution of these costs in Argentina in 2020. Diagnostic services (mammograms and ultrasounds) accounted for 5% of the total direct costs. Surgery and radiation therapy accounted for 4% and 7% of the costs, respectively. Cancer medicines, in particular chemotherapy, CDK4/6 targeted therapies for hormone-sensitive breast cancers and HER2-targeted therapies for HER2-positive breast cancers, accounted for most of the remaining costs. It is not unexpected that immunotherapies make up only a small portion (0.1%) of total direct expenses, considering that the country's first immunotherapy for breast cancer received regulatory approval in 2019 (97).





**Figure 19: Direct medical costs of breast cancer care in Argentina in 2020.** Source: (98).

As breast cancer advances, the breakdown of direct medical costs evolves significantly. Figure 20 presents findings from research that aimed to delineate the expenses associated with metastatic TNBC patients in Costa Rica. The estimated direct medical costs per year per patient were 17,314 USD. Health care services and chemotherapy represented the largest shares of these costs, at 36% and 27% respectively. Additionally, the need for supplementary supportive care is evident in the advanced stages, as highlighted by the increased use of palliative care. Surgery and radiotherapy are utilized less frequently in these later stages, indicating a shift in treatment strategy.

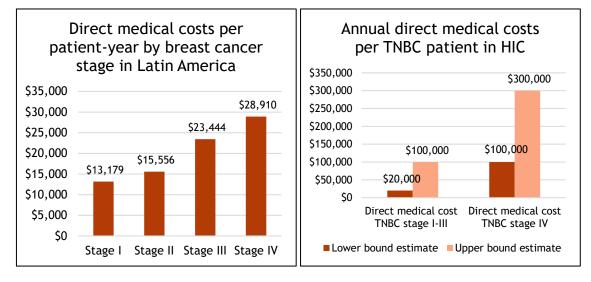


## Figure 20: Direct costs of metastatic TNBC in Costa Rica in 2019.

Notes: The study made an estimation of metastatic TNBC cases and costs. In that year there were 284 new cases of TNBC and 25 of them were metastatic. Source: (99).

Several studies from Latin America show that the direct medical costs of breast cancer increase considerably in advanced stages due to more complex and intensive treatments (100-102). A systemic review of studies across the region showed that the per-patient-year costs for stage IV breast cancer are more than twice as much as for stage I (102); see Figure 21. Similarly, a more recent study of one of Mexico's largest public health providers found that costs for stage IV breast cancer patients are three times higher than costs for stage I patients (100).

A similar pattern of late-stage patients being around three to five times more costly than earlystage patients to health care systems on an annual basis has also been found for TNBC in a systematic review of HIC (103); see Figure 21. The per-case cost of treatment for TNBC in a recent study for Canada varied even more, from C\$ 25,247 in stage I to C\$ 101,811 in stage II, C\$ 110,798 in stage III, and C\$ 193,490 in stage IV (104). These cost differences between disease stages underline the economic importance of early detection of breast cancer. Increasing the proportion of women diagnosed in early stages, which is a major challenge in Latin America (see section 4.2), would not only save lives but also health care costs.



# Figure 21: Direct medical costs of breast cancer per patient-year by stage in Latin America (in Int\$) and Range of average annual direct medical costs per TNBC patient by disease stage in HIC (in 2021 USD).

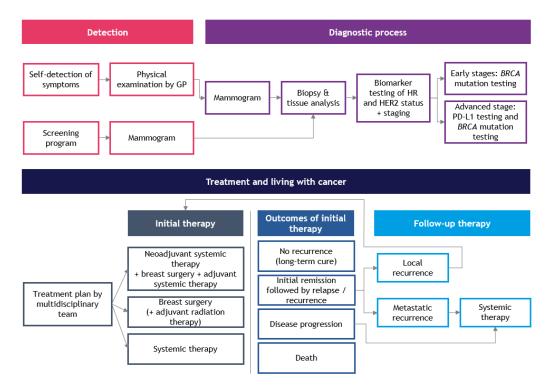
Notes: The numbers shown for Latin America are pooled, weighted averages of individual studies covering Brazil, Colombia, Ecuador, Mexico, Peru, and Puerto Rico. The numbers for HIC were gathered from Belgium, Canada, Spain, France, Portugal, Sweden, and the United States. Source: (102, 103).



## 4. Challenges in TNBC care

The provision of high-quality care to TNBC patients consists of many elements. Fundamental factors that affect countries' abilities to provide equal and high-quality care to the entire population are the financing of the health care systems and health insurance coverage (see section 4.1).

TNBC-specific challenges can be found along the entire patient pathway; see Figure 22. The first key stage of the pathway is the detection of breast cancer, which can be triggered through self-detection or through screening (see section 4.2). The second key stage is the diagnostic process, which contains a biopsy to confirm the diagnosis, staging, and biomarker testing in order to be able to select adequate treatment options (see section 4.3). The third key stage is treatment (see section 4.4).



### Figure 22: Stylized patient journey in TNBC.

Notes: Based on American Cancer Society and ASCO, ESMO, and NCCN guidelines. The classification "systemic therapy" includes chemotherapy, immunotherapy, and targeted therapy. Source: (105-108).

In 2021, the WHO established the GBCI to provide strategic guidance and coordination aimed at improving breast cancer care, with a focus on low- and middle-income countries (109). The aim is to reduce global breast cancer mortality by 2.5% per year, thereby averting 2.5 million breast cancer deaths globally between 2020 and 2040. The three pillars toward achieving this aim correspond to the key stages depicted in Figure 22.

- 1. Health promotion for early detection (pre-diagnostic interval)
  - KPI: >60% of cancer cases are stage I or II at diagnosis.
- 2. Timely breast cancer diagnostics (diagnostic interval)
  - KPI: diagnostic evaluation, imaging, tissue sampling and pathology within 60 days.
- 3. Comprehensive breast cancer management (treatment interval)



• KPI: >80% undergo multimodality treatment without abandonment.

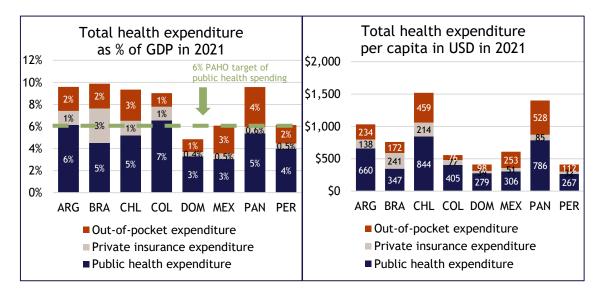
The following sections provide insight into the health systems in the countries under study and elaborate on some of the most significant obstacles faced in each of these three domains.

### 4.1 Health system readiness

Most Latin American countries analyzed in this report started reforming their health systems in the 1990s to achieve universal health coverage (UHC) (110, 111). Even though UHC in terms of covering the entire population has been a priority for all countries, there are persistent challenges in ensuring access to and affordability of health care services. The growing demand for health care due to population aging adds additional pressure on the health care systems. The WHO's index of essential service coverage for 2019 shows varying levels across countries. The Dominican Republic scored 66 out of 100, followed by Argentina with 73, Mexico with 74, Brazil with 75, Panama with 77, and Peru and Colombia both with 78 (112). Leading the list, Chile scored 80 points. These data indicate that a significant portion of the demand for these services remains unmet. In comparison, Spain had an index of 86 points and Canada 89 points (112).

### Health spending

The monetary resources invested in health care differ across Latin American countries. Argentina, Brazil, Panama, Chile, and Colombia spend around 9-10% of their gross domestic product (GDP) on health care, while the Dominican Republic, Mexico, and Peru only spend around 5-6% (113, 114). Figure 23 shows how the public portion of total health spending falls short of the Pan American Health Organization's (PAHO) recommended 6% in Brazil, Chile, the Dominican Republic, Mexico, Panama, and Peru (115). The public expenditure also falls short of the informal WHO-target of 5% public spending in Brazil, the Dominican Republic, Mexico, and Peru. In absolute numbers, Chile is spending around \$1,500 per capita on health care, compared with around \$600 in Colombia and Mexico, and \$400 in the Dominican Republic and Peru. Mexico and Panama are the countries where out-of-pocket expenditure is almost as large as public expenditure, indicating a large financial burden for patients.



### Figure 23: Total health expenditure as percentage of GDP and in USD per capita in 2021.

Notes: GDP = gross domestic product. Expenditure figures are not adjusted for purchasing power parity differences. External health expenditure was excluded. According to the latest 2022 OECD data available



at the time of this report, Chile's current health expenditure is 9% of its GDP, while Colombia and Mexico report slightly lower numbers than those for 2021 at 8.1% and 5.5% of GDP, respectively. Source: OECD and WHO (113, 114).

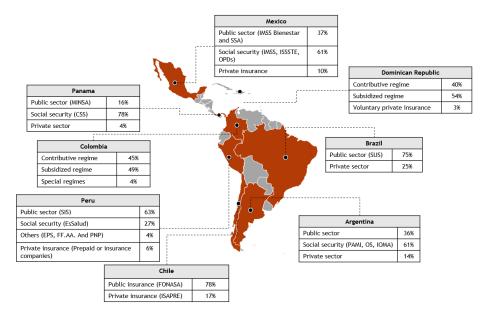
Public health expenditure on cancer care is limited in the region. In Chile, 3% of the planned public health care budget was allocated to cancer care in 2022 (116). In comparison, around 6% of total health expenditure was spent on cancer care in Europe in 2018 (117).

#### Health insurance coverage

In addition to being underfunded, the health care systems in Latin American countries are also highly fragmented; see Figure 24 showing the primary providers of health insurance coverage in each country. Argentina, the Dominican Republic, Colombia, Mexico, Panama, and Peru all have health care systems that consist of social security regimes for both employed and self-employed individuals, private health insurance options, and a public health care system designed to serve vulnerable populations, including informal workers and immigrants. In Brazil and Chile, the health care system is divided into public and private coverage. Each of these regimes has different funds and allocates its resources differently. The reliance on the private sector greatly affects lower socioeconomic groups, which have limited ability to pay, and perpetuates inequalities in access to health care.

For breast cancer care, the fragmentation of the health systems creates two challenges. First, it undermines the effectiveness of national breast cancer prevention initiatives. Second, it creates profound inequalities by provisioning health services according to insurance coverage.

Even within the public sector, the comprehensiveness of health coverage and quality of care can differ drastically within institutions from different regimes, leading to a completely different patient journey. For example, in Colombia, only 9% of women in the subsidized regime are diagnosed at stage I, compared with 18% of women in the contributory system (118). 12% of women are diagnosed at stage IV in the subsidized system, compared with only 6% in the contributory system (118).





Notes: The data for Argentina are from 2021. For Brazil, the data for private insurance correspond to 2021, while the data for public insurance are from 2019. For Chile, the data are from 2020 and for





Colombia from 2022. For Mexico, the data for the public sector and social security are from 2020, while the data from private insurance are from 2021. Panama data for CSS are from 2021, for MINSA from 2014, and for private insurance from 2019. The data for the Dominican Republic regarding the contributive and subsidized regimes is from 2022, while the information on private insurance is from an unpublished 2018 IQVIA report. This report estimated that 368,779 individuals had voluntary private insurance apart from the contributive regimen. Peru data is from 2023. Source: (119-133).

#### **Cancer registries**

- Argentina boasts the Institutional Tumors Registry of Argentina (RITA), a hospital-based cancer registration system that was put into operation in 2012 (134). Currently, 29 institutions actively contribute data to RITA. While RITA generally maintains commendable levels of data completeness, particularly in areas such as sociodemographic information and tumor sites, it does face certain challenges (135). During the period between 2012 and 2018, tumor stage information for breast cancer cases was incomplete, with nearly half of the cases having an unknown stage (135).
- In Brazil, there are 30 well-structured population-based cancer registries primarily funded by the municipal authorities (136). Despite robust infrastructure, only a handful of these registries have had their data featured in recent volumes of Cancer Incidence in Five Continents by IARC (136). Registries from 2000-2014 only covered close to 8% of the national population (7).
- Chile lacks a national cancer registry, yet five regional population-based cancer registries existed in 2020 (137). Notably, none of those were situated in Santiago, the capital city that houses a large segment of the nation's population (137). Registries from 2000-2014 only covered close to 14% of the national population (7).
- In Colombia, the IARC-accredited population-based cancer registries were estimated to cover only 12% of the country's population in 2019 (138). For comparison, cancer registries in Europe cover on average of 60% of their populations (139).
- In the Dominican Republic, insufficient data within hospital registries, particularly the lack of cancer staging information, poses a significant obstacle to comprehensive cancer research and health care planning. Data from the two main oncology institutes show a deficiency in capturing cancer staging information. Data from the Instituto Nacional del Cáncer Rosa Emilia Sánchez Pérez de Tavares (INCART) for 2019 revealed that 77% of breast cancer cases had no recorded stage (14). In 2020, this number increased to 97%, and in 2021, a staggering 98% of cases lacked staging information. Data from the Instituto de Oncología Dr. Heriberto Pieter (IOHP) in 2017 showed that 17% had no recorded stage (140).
- In Mexico, the design of the National Network of Cancer Registries (NNCR) began in 2017 with a network of 10 population-based registries covering 12% of the population, aligned with IARC standards. However, the registry was deactivated in 2022 due to a lack of funding (141).
- Despite Panama having a National Cancer Registry that encompasses 77% of health care institutions offering oncology services, it still falls short of delivering comprehensive and high-quality data (142). A study of breast cancer cases, spanning from 2012 to 2016 and using information from the National Cancer Registry, revealed that less than half of the cases (1,787 out of 4,134) contained staging information, and there was an absence of data pertaining to tumor biology, specifically the presence of hormonal receptors (94). The researchers attributed this incompleteness in part to delays in



reporting cases from the National Oncology Institute (ION) and rural communities to the Ministry of Health.

• In Peru, there are population-based cancer registries operating in Lima, Trujillo, and Arequipa, collectively covering 34% of the population (143). Despite this relatively extensive coverage compared with other countries assessed in this report, these registries also had certain issues concerning data quality and completeness. In 2021, only 57% of the registered cases included information on the clinical stage of cancer (144).

### 4.2 Challenges in early detection

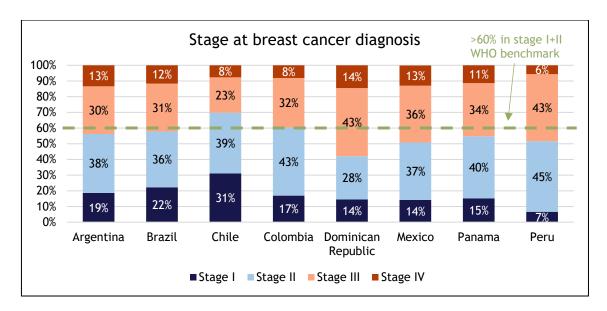
Generally, breast cancer is detected in two ways. First, a woman may detect/experience symptoms (see section 2.3) and then consult a health care professional for diagnostic confirmation. Second, women who fall into the target age group for a breast cancer screening program may have an asymptomatic tumor detected on their mammogram.

The 1st edition of the Latin America and the Caribbean Code Against Cancer, published in 2019 and coordinated by the IARC and PAHO, includes actions aimed at early detection of breast cancer (145, 146). Endorsed by specialists and civil society, the Code includes recommendations for women aged 40 and older to schedule a clinical breast exam with a health care provider every two years. It further recommends that women between the ages of 50 and 74 undergo a mammography every two years. Self-examination alone as an early detection method is discouraged, as it is not considered beneficial.

In Latin America, awareness of symptoms to facilitate self-detection is critical as most countries lack effective screening programs with mammography. While in HIC around 50% of breast cancer cases are detected through screening (147), this proportion is lower in Latin America. For example, 84% of breast cancer cases in Mexico are diagnosed after women have started to develop symptoms (148). In Peru, approximately 93% of cases are diagnosed when they manifest symptoms (149). In Chile, 68% of non-TNBC cases and 85% of TNBC cases were detected based on signs and symptoms from 2010-2021 (23).

The lack of screening programs and/or low participation in these programs in Latin America hampers efforts to detect breast cancer early and contributes to a high percentage of cases being diagnosed at an advanced stage. Figure 25 shows the stage distribution at breast cancer diagnosis per country. It also includes the target by the WHO GBCI of diagnosing at least 60% of cases in stages I and II. Of all countries analyzed, only Chile surpasses this target, although it missed the target for TNBC with only 58% of cases diagnosed in stages I and II (23).





#### Figure 25: Stage distribution of breast cancer at diagnosis and WHO target.

Notes: Data for Argentina were obtained from the Institutional Registry of Tumors (RITA) and cover cases diagnosed in 2012-2018 (n=9,900) and were extrapolated excluding the "desc" category that were 46% of cases. Data for Brazil include cases from the hospital-based cancer registries in 2019 and were rescaled without in situ cases. Data for Chile include cases from a public community hospital and an academic private hospital in 2010-2021 (n=5,806). Data for Colombia include all newly diagnosed cases treated in the public sector in 2021 (n=5,468). Data for Mexico include all patients diagnosed at the National Cancer Institute (INCan) with Seguro Popular in 2007-2013 (n=4,300). Adjusted data for the Dominican Republic is for patients treated at the INCART in 2019 (n=296) with 227 unknown cases. Data for Panama from the National Cancer Registry from 2012-2016 (n=1,768). Data for Peru shows cases from INEN (n=1,943). Sources: (12-14, 23, 94, 118, 135, 150, 151).

Figure 26 summarizes key challenges identified for early breast cancer detection in the included countries in Latin America. While not all challenges apply to each country, they appear in at least one of them. A detailed description of the challenges is provided below.

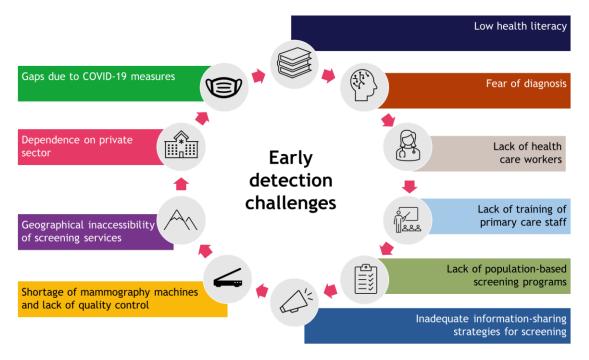


Figure 26: Challenges in early detection of breast cancer in Latin America.



### Challenges relating to self-detection

#### Low health literacy

- According to a 2021 survey of 7,000 women from various Latin American countries— Argentina, Chile, Colombia, Mexico, and Peru—51% believe self-examination to be the most effective method for detecting breast cancer, surpassing mammography, which only 30% of respondents considered to be the most effective (152).
- Low awareness of less frequent early signs of breast cancer, such as inverted nipples or skin changes were only known by 47% and 41%, respectively, of the women in the survey mentioned above (152).
- 1 in 4 women in Latin America depend on their clinician's advice to undergo mammography. This indicates a failure of screening programs to entice women to attend breast screening out of habit (152).
- In Peru, a study conducted in 2015 among women in the Lower Napo River region, which has a sizable indigenous population, revealed low levels of breast cancer awareness (153). 24% of the participants had never heard of breast cancer. Only 32% were able to identify one of the main symptoms, and none of the participants were aware of any early detection activities such as regular breast examinations.
- In Chile, the lack of knowledge and understanding about genetic issues and their relevance in medical care has been documented among health care professionals and the general public (154).

#### Fear of diagnosis

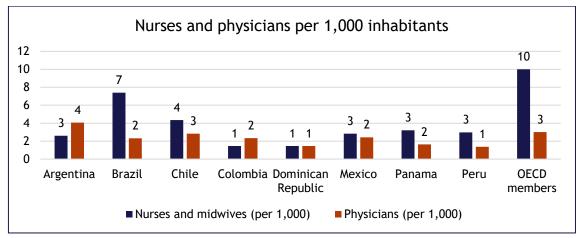
- A study in Colombia found that 13% of women who abstained from undergoing a mammogram cited fear of diagnosis as the main reason (155). Similarly, an estimated 9% of Mexican women who do not undergo a mammogram are driven by the fear of diagnosis (156).
- A qualitative study in Panama revealed that many women felt as though they had received a death sentence upon diagnosis, largely due to their limited understanding of breast cancer (157).
- In Peru, a study found that the most frequent reason for avoiding a mammogram was fear of the diagnosis (59% of the sample) (149). Also, a qualitative study revealed that women frequently experience apprehension not only about their own diagnosis but also about the potential impact on their children, especially among mothers with young children (158). Additionally, the women in the study expressed fears associated with changes in their bodies (158).

#### Lack of health care workers

- All countries, with the positive exception of Argentina and Chile, had a ratio of practicing physicians per 1,000 inhabitants lower than the average for the OECD; see Figure 27. All countries had a ratio of nurses and midwives per 1,000 inhabitants much lower than the average of the OECD members.
- The OECD has identified the shortage of physicians as one of the primary challenges in primary care in Brazil (159).



- In Chile, an insufficient number of primary care providers have been reported to be one of the reasons leading to long waiting times for women to receive a breast cancer diagnosis (160).
- In Panama, shortages of primary care physicians have been recorded (161).
- In the Dominican Republic, there is not only a shortage of nurses and physicians but also a significant disparity in their distribution. The National Health System (SNS) in 2019 showed that in the Northeast region there were 17.5 physicians per 10,000 inhabitants while the Valdesia region had only 12.1 (162). Regarding nurses, there were 7.2 per 10,000 in the Enriquillo region, compared with 2.1 in the East region.
- In Peru, health care personnel shortages are exacerbated by absenteeism and administrative issues (163). A study conducted in Lima observed that 10% of healthcare primary providers (doctors, nurses and midwives) were unexpectedly absent for shifts they had confirmed they would attend a week prior (164). Additionally, a similar number of providers switched their shifts after the schedules were set. These unplanned absences and shift changes disrupt the effective organization and provision of healthcare services(164). Also, there was a substantial loss of productive time in clinical activities due to the necessity of maintaining paper records for both clinical and administrative purposes (164).



### Figure 27: Nurses and physicians per 1,000 inhabitants.

Notes: For the sake of consistency, the most recent data used in this graph is obtained from the World Bank. The data for Argentina pertains to the years 2017 and 2020, while data for Brazil, the Dominican Republic, Mexico, and Panama is from 2019. Chile and Colombia's data is from 2020, and Peru's data is from 2018. Source: (165).

### Lack of training of primary care staff

- A study on the challenges of early breast cancer diagnosis in Chile revealed that many primary care providers have limited exposure to breast cancer patients and are not fully up-to-date on clinical practice guidelines. This lack of experience stems from limited encounters with breast cancer during their medical training and inadequate training in their day-to-day practice (160).
- A study conducted in Mexico at two public hospitals found that younger women showing symptoms of breast cancer were at a higher risk of not being promptly referred from primary care to diagnostic services compared with older women (166). The longer



diagnostic intervals were mainly due to physicians at the initial point of contact in the health care system not suspecting breast cancer.

• In a qualitative study conducted in Peru, it was noted that women were frequently misdiagnosed with fat deposits or a benign lesion or fibroadenoma instead of being correctly diagnosed with cancer (158).

### Challenges relating to screening

An overview of key features of the breast cancer screening strategies in the included countries as well as participation in the screening programs is provided in Table 5. Most countries fall short of reaching their target population for screening ( $\approx 30\%$ ), with Chile being a notable exception. There have been encouraging developments aimed at improving screening rates. For instance, in Peru, Law N° 31561 was approved in 2022 (167). This legislation aims to provide female workers, regardless of whether they work in the public or private sector, the right to take leave for the early detection of breast cancer (167). This leave is designated as one day per year, specifically for early detection examinations. However, although the law has been approved and enacted, the specific regulations that detail how it will be implemented and applied in practice are not yet available in 2023.

Country	Early detection strategy	Target population	Results
<b>o</b> Argentina	-The public health care system subsidizes mammography screening and clinical breast exams (168).	-Women aged 50-69, mammography every one or two years. -Screening for high-risk women under 50 (such as those with a first-degree relative who has had breast or ovarian cancer).	-32% of the target population gets screened (24). -30% of breast cancer diagnosed at late stages (168).
Brazil	-Screening is free for the target population (169). -Self-examination is not recommended as a screening method (170) but still many health care professionals teach self- examination techniques (171).	-Women aged 50-69, mammography every two years.	<ul> <li>-32% of women aged 50- 59 and 25% of the group 60-69 get screened (172).</li> <li>-The availability of mammograms has increased in recent years (173).</li> <li>-40% of breast cancer cases are diagnosed at late stages (174).</li> </ul>
<b>*</b> Chile	-Screening is free for the target population (covered by Fonasa or Isapre) (175).	-Women aged 50-59 (previously 50-69), mammography every three years (175). -Women in high-risk groups outside of this age interval can also receive mammograms.	-Around 71% of women aged 50-59 report to have had a mammography during the last three years (176), but screening detected cases are low (32% in non-TNBC and 15% in TNBC) (23). -Significant disparities across socioeconomic groups, with a screening rate of only 34% in low

### Table 5: Breast screening programs and results



			socioeconomic groups (177).
Colombia	-Screening for breast cancer is provided at a population-level.	-Women aged 50-69, mammography every two years (12). -Annual clinical breast exam starting at age 40.	-Close to 30% of the target population gets screened, with significant disparities across regions (178). -33% of cases are diagnosed in stage III and IV (151).
Dominican Republic	- Breast cancer screening is free through the Early Detection Program for vulnerable populations (179, 180).	-Women aged 40-65 years every year with mammography (179, 181, 182).	-In 2013, a study estimated that the breast cancer screening participation rate was around 10% (183). -In 2019, based on available diagnostic data at INCART, 58% of breast cancer cases were detected in stages III and IV (14).
کی اور	-Due to the fragmented health system, screening programs are not carried out at a national level. -Opportunistic screening as emphasis is placed on self- examination.	-Women aged 40-69 are encouraged to get screened, but the responsibility falls on them. -Self-examination is advised for women as of age 20-25.	<ul> <li>-15 to 25% of the target population gets screened (184, 185).</li> <li>-80 to 90% of cases are diagnosed after stage IIB (184).</li> </ul>
Panama	- According to Law 32, mammographies are provided free of charge in the public sector for both insured and uninsured women (186).	-Women aged 40-74 years every two years with mammography (187).	-A study using data from the National Cancer Registry found that close to 45% of breast cancer diagnoses were in stages III and IV (94).
Peru	-The Comprehensive Health Insurance system (SIS) and EsSalud cover detection of breast cancer for affiliated women (188).	<ul> <li>-Women aged 40-69 years with clinical breast examination annually (189).</li> <li>-Women aged 50-69 years are recommended to get a mammography every two years (190).</li> <li>-Women aged 70-74 years with a mammography after an individual assessment of harms and benefits (190).</li> </ul>	- According to the National Institute of Statistics, around 8-10% of women aged 50-69 had undergone a mammogram within the last 24 months in both 2021 and 2022 (191). -A study found that close to 48% of cases were in stage III and IV (13). Other studies estimate a higher proportion of around 53% (192).

#### Lack of organized population-based screening programs

• Screening programs are formally in place in many countries, but they are more opportunistic than organized; see Table 5. Organized systems actively and individually invite all women of the target age group to screening - ideally also defining a time and place for the screening - drawing on centralized population registers, and also using a uniform call-recall system (193). In Latin American countries, it is often left to women themselves to understand that they are eligible for screening and to approach health services and make an appointment.

- In Mexico and Peru there is no organized mammography screening (148). In Mexico, there are separate efforts, but not a coordinated single national program. Units of Medical Specialties for the Detection and Diagnosis of Breast Cancer (UNEME-DEDICAM), for example, are only available in a few Mexican states (194).
- Some existing screening programs appear fragmented, such as in Brazil, which creates inequalities in access. This might partly explain the low Brazilian screening rates in the North compared with the Southeast (172).
- Despite Panama's Law 32, which mandates free mammographies, and the presence of various annual screening campaigns, the nature of these screenings continues to be opportunistic (186).

#### Low participation in screening programs

- Participation rates in breast cancer screening programs in most countries are around 10-30%, with the positive exception of Chile; see Table 5. This is much lower than in HIC; e.g., the average participation rate was 66% in women aged 50-69 years in the European Union and 76% in women aged 50-74 years in the United States in 2019 (195, 196). Participation is even low in Latin American countries where screening is subsidized or free.
- While there is a lack of data regarding screening participation rates in the Dominican Republic, the period spanning 2020-2022 saw only 82 women, who were undergoing breast cancer treatment at the Instituto Nacional del Cáncer Rosa Emilia Sánchez Pérez de Tavares (INCART), enrolled in the Early Cancer Detection Program (PDOC), indicating low participation rates (14). As this program is relatively new, the situation may improve over time. Nevertheless, low participation in breast cancer screening had been witnessed already in the years preceding the new program, with a study from 2013 estimating a participation rate of just 10% (183).

#### Narrow target age group in screening programs

• The target age group for mammography in most countries consists of women aged 50-69 years; see Table 5. This is a narrower target age group than the 50-74 years recently recommended by PAHO and IARC in the Latin America and the Caribbean Code Against Cancer. The United States Preventive Services Task Force recommends the age group 50-74 years and the European Commission recommends 45-74 years (197, 198). As a larger proportion of women in Latin America develops breast cancer at younger ages than in Europe and the United States (see Figure 3), the lower limit of 50 years excludes a sizable group of breast cancer patients, and in particular TNBC patients.

### Inadequate information-sharing strategies for screening

- A study in Colombia analyzed national data from 2005, 2010 and 2015 to investigate the performance of early detection activities, including breast cancer screening. The study revealed that among the most common reasons for not participating in early detection activities were a lack of clarity about which health care facility to visit and long waiting lists for appointments (199).
- A study on the challenges of early breast cancer detection in Chile identified that the promotional communication strategies for the breast cancer screening program were inadequate, both in terms of frequency and content. In terms of frequency, they were considered insufficient, as they mainly focused on the month of October. Regarding



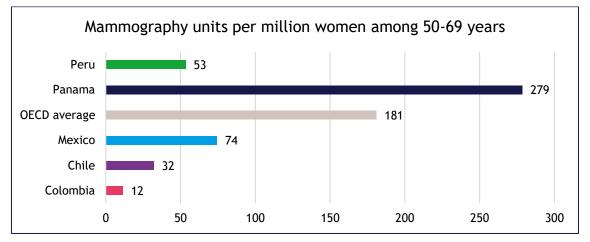


content, they failed to explain the benefits of early diagnosis or adequately inform Chilean women about their available health care options (160).

• Locating information on breast cancer screening initiatives within Peru's public sector can be difficult. Although the official MINSA website (for SIS) lists health centers that offer mammography services, its description ambiguously states that a mammogram is necessary "if you need to undergo one" (200). Such phrasing might deter some women from pursuing mammograms unless they experience symptoms.

#### Shortage of mammography machines and lack of quality control

- In Chile, the public system lacks sufficient mammography equipment. Therefore, services are outsourced to the private sector, where providers are selected primarily based on their prices, leading many times to sacrificing quality for price (160).
- The OECD reports an average of 181 mammography units per million women aged 50-69 years (201). However, as illustrated in Figure 28, Mexico, Peru, Chile, and especially Colombia has significantly fewer units per million women in this age bracket, falling below the OECD average. Conversely, Panama stands out as a positive exception, boasting a higher number of mammography units per million women among this age group compared with the OECD average.



#### Figure 28: Mammography units per million women among 50-69.

Notes: latest date available which for Colombia, Chile and Mexico was 2019 and for Panama 2016. Data for Peru was estimated for the year 2023 utilizing information about the 146 mammography machines available for the Ministry of Health and EsSalud divided by all women aged 50-69. Source: (201-203).

• Even when mammography machines are available, if they are not functioning properly, women cannot receive reliable screenings. Several studies in the region have reported low quality of mammography that leads to poor accuracy of clinical diagnosis, leading to repeated tests, raising costs in the long run and causing delays in early detection. Estimates for Argentina indicate that 40.7% of mammography equipment continues to use analog technology, which has lower image resolution than digital technology. In Brazil, 40% of all mammography machines are estimated to be working at inadequate levels of quality, increasing the risk of incorrect diagnosis (172). In Chile, the estimated percentage of inconclusive mammography results in Santiago was 23.3% while in the United States it was close to 9.7% in 2019 (160). As a result, even if screening rates



improve in the future, there is considerable uncertainty about the reliability of test results.

- In 2023, a media outlet in Peru conducted an analysis revealing that EsSalud possessed a total of 76 mammography machines. Of these, only 34% were considered to be in "good" condition, 40% were described as in "regular" condition, and the remaining 17% were evaluated as being in either "bad" or "regular to bad" condition (203). The analysis also noted that the MINSA (for SIS) had 70 mammography machines (203). Although, by the end of 2023, MINSA had supplemented its inventory with 29 new mammography machines (205).
- In the Dominican Republic and Panama, mammography units lack quality accreditation (181, 187).

#### Geographical inaccessibility of screening services

- Some women may face difficulties accessing clinics due to an uneven geographical distribution of clinics and equipment, especially if they live in remote areas or are members of low socioeconomic groups who must spend a larger proportion of their income on transportation. In Mexico, the screening participation rate for women living in cities was 32% in 2013, while women in rural areas had a lower rate of 17% (206). Although more recent data was not found, press releases from 2020 also highlighted lower mammography rates in rural areas in some states of Mexico (207).
- In Brazil, according to the 2021 Guide for Best Practices in Navigating Patients with Breast Cancer, only 24% of the country had geographic coverage for mammography screening, well below the WHO's recommendation of at least 70% (208). Therefore, even if the total number of mammography machines is sufficient, the number of mammograms performed will still be insufficient if those machines are not easily accessible to women all across the country (209).
- Some studies have found significant differences in breast cancer incidence rates across Argentinian regions, which have been linked to the fact that specialized health facilities are concentrated in large cities (168).
- The Dominican Republic introduced the Early Cancer Detection Program (PDOC) within the National Health Service in 2021, functioning across ten hospitals and mobile units (210). Although data published in 2023 indicate that 33,212 women received diagnostic screenings, including mammographies, between 2021 and 2023 (211), it is important to note that this program is currently only accessible in specific hospitals, and does not cover the whole country. Feedback from the screening campaign reveals that many patients are advocating for the program's expansion to include more hospitals in their respective regions (179).
- In Panama, a qualitative study from 2014 for women in rural communities who are part of indigenous populations revealed that they find health care service hours to be inadequate, as they did not cater to their actual needs (157). The timings did not take into account the distances they needed to travel to access the services and then return to their homes. In this study, interviewed health care personnel indicated that distance and transportation costs were the main barriers for early detection.
- In Peru during 2021-2022, the mammogram rate for urban women aged 40 to 69 was only 11%, significantly lower than in regional countries like Chile (70%) and Colombia (30%) (191). This is far below the 2016 EsSalud guideline's goal of 70% screening in the





targeted age group (50 to 74 years) (212). The situation is more severe in rural areas, with only a 3% participation rate (191). Additionally, a 2023 Peruvian media analysis revealed a notable disparity in mammography equipment availability, particularly in regions like Tumbes, Pasco, and Madre de Dios, where there is no access to such equipment in MINSA-affiliated hospitals (203).

#### Dependence on private sector

- In Colombia, a study revealed that in 2010, 13% of women paid for mammograms in the private sector (199). Additionally, 20% of women with coverage under the subsidized regime also paid for their mammograms.
- In Mexico, important differences between women treated in the public and private health care sector have been recorded. A study found that 83% of women treated in the public sector were diagnosed based on symptoms compared with 48% in private facilities (11). Also, 31% of women accessing the public sector were diagnosed at a late stage, compared with 18% in the private sector.
- In Argentina, a study in the private sector revealed that 42% of breast cancer cases were diagnosed at stage I, and 14% at stage IV, while in the public sector, only 17% were diagnosed at stage I and 31% at stage IV (98) Similarly, in Brazil, a study revealed that approximately 40% of cases were diagnosed at advanced stages (III, IV) in the public sector, compared with 16% in the private sector (172).
- In Chile, patients in the public sector are more likely to be diagnosed at advanced stages and must wait longer for treatment initiation than in the private sector (213).

#### Gaps due to COVID-19 measures

- All Latin American countries have reported decreases in breast cancer screening rates due to the inaccessibility of services during the COVID-19 pandemic. This might lead to more late-stage diagnoses in the coming years.
- Some locations in Argentina reported lower screening rates of between 56-87% and lower diagnosis rates of 26% in 2020 compared with 2019 (214). In Brazil, the number of mammograms performed in the public sector decreased by 42% in 2020 and 15% in 2021 compared with 2019 (215). In Chile, there was a decrease of 62% in breast cancer diagnosis in 2020 compared with 2019 (216). In Mexico, breast cancer screening declined by 79% in 2020 compared with 2019 (217). In Peru the breast cancer screening in 2020 decreased 51% compared with the screening rate in 2019 (218).

## 4.3 Challenges in the diagnostic process

Breast cancer is diagnosed with a triple assessment that involves a physical examination, a mammography/ultrasound imaging and a biopsy (147). Mammography, which is a low-dose X-ray imaging method, is the most common method to diagnose breast cancer. Radiologists analyze the images (called mammograms). A breast biopsy to obtain a sample of breast tissue is performed if the imaging test results indicate the possibility of breast cancer. The sample is then examined by a pathologist to determine tumor characteristics. This process also involves biomarker testing of hormone receptor and HER2 status in order to determine the breast cancer subtype. Together with information on the stage, the most suitable therapeutic approach can be decided. For TNBC in particular, novel treatment options require additional biomarker testing of PD-L1 status in metastatic patients prior to treatment initiation. As of 2022, international clinical





guidelines by ASCO, ESMO, and NCCN recommend these novel biomarker tests as part of the diagnostic process (107, 108, 219).

Apart from being comprehensive, the diagnostic process should be swift. Keeping the time between diagnosis and start of treatment as short as possible increases the chances of survival (220). Breast cancer patients with a long delay of  $\geq 61$  days between diagnosis and start of neoadjuvant systemic therapy (i.e., the therapy performed before surgery) have a 28% increased risk of subsequent mortality compared with patients with a short delay of 0-30 days (221).

Figure 29 summarizes key challenges associated with the diagnostic process of TNBC in the included Latin American countries. Note that not all challenges apply to every country.



#### Figure 29: Challenges in the diagnostic process of TNBC in Latin America.

#### Poor coordination of diagnostic service providers

- In Mexico, the lack of clear referral routes for women with breast cancer symptoms receiving care in the public system is one of the main reasons for long waiting times for diagnosis (166). This situation and the long waiting times entice women into having some diagnostic tests performed in private facilities, necessitating out-of-pocket payments. Finally, patients often find themselves needing to repeat diagnostic tests at public health centers due to the low quality of service of some private sector providers (222).
- In Chile, poor coordination between primary and secondary care levels impede timely referrals and contribute to long wait times (160).

#### Unnecessary surgical biopsies

• In Panama, through a needs assessment conducted by the Breast Health Global Initiative and Susan G. Komen, it was revealed that the predominant biopsy method used at second-level facilities involved excisional procedures rather than core needle biopsies (223). Excisional biopsies entail the surgical removal of either the entire tumor or a substantial portion of it for examination, necessitating the involvement of a surgeon and, consequently, causing significant delays in the diagnostic process.



#### Long delays to get diagnostic results

- In Peru, a study with data from an EsSalud hospital in Lima highlighted delays in the diagnostic process for breast cancer. The study found that the average time from when a patient receives a mammogram result indicating a suspicion of breast cancer to when they receive an anatomic pathology diagnosis confirmed by biopsy was 81 days, with the mean duration being 159 days (224). In total 78% of the sample exceeded the 60-day benchmark for the entire diagnostic process set by the WHO GBCI's second pillar.
- In another study with data from Peru and Mexico, it was found that 60% of all breast cancer patients had a diagnostic delay of more than 3 months (148). The median time from medical consultation to diagnosis in Peru was 174 days and in Mexico 113 days.

#### Shortages of radiologists and pathologists

In Latin America, the demand for breast imaging generally exceeds the available workforce, which is exacerbated by insufficient training. The countries are facing the following difficulties:

- In Argentina, there are shortages of radiologists (204). These shortages lead to long waiting times for essential diagnostic services and thus compel women to rely on services in the private sector with the risk of high out-of-pocket expenditure (225).
- In Brazil, shortages in the breast imaging workforce lead to long diagnostic delays. According to the 2021 Guide for Best Practices in Navigating Patients with Breast Cancer, based on data from Sao Paulo, the average time to obtain anatomopathological test results is 74 days (208).
- Colombia suffers from a serious shortage of pathologists, as there are only around 500 general pathologists in the whole country to cover all 51 million inhabitants (226).
- In Mexico, there are approximately 3 radiologists per 100,000 inhabitants, which is lower than in Brazil with 5.8 radiologists per 100,000 inhabitants and where also shortages exists (227). In Europe, there are 13 radiologists per 100,000 inhabitants (228). In all of Mexico, there are only 587 radiologists accredited for breast imaging (229).
- In Panama, a deficit of 200 radiologists was identified in 2012 (230).
- In Peru, as of 2017, there were 113 radiologists, with only 28% of them having received training in mammography (231). Adding to this challenge, there were 162 radiographers responsible for capturing the images, resulting in a ratio of 1.6 radiographers per radiologist, which falls short of the recommended PAHO ratio of 2.5 (231).

#### Insufficient education and training of radiologists and pathologists

- In Chile, few undergraduate pathology courses address breast cancer and there are few possibilities for internships in breast pathology units (160).
- In Argentina, the training of radiology technicians often does not incorporate new technologies (204).
- In Peru, a study from 2015 of the quality of 772 public and private clinical laboratories revealed that 56% of the laboratories did not have training plans for their staff (232).



#### Lack of diagnostic infrastructure

- In Brazil, a shortage of pathology laboratories within hospitals causes tissue samples to be transported to external laboratories. This creates numerous opportunities for quality failures, leading to a need for re-biopsy if the tissue sample is compromised (233).
- Some public laboratories in Brazil do not offer basic molecular testing for hormone receptor status and HER2. Patients will have to pay out-of-pocket if they wish to have the tests done at a private laboratory (234).
- In Chile, pathological tests are often not performed in-house but instead sent to different centers, potentially delaying diagnosis (160).
- In Chile, *BRCA* tests in patients with a hereditary breast cancer have been recommended in national clinical guidelines, but the lack of molecular diagnostic equipment, insufficient numbers of qualified human resources and insufficient funding make it difficult to implement this recommendation (235).
- In Peru, as of 2017, 15 departments reported a lower-than-national-average availability of pathological anatomy services in public health facilities (236). Notably, some departments, including Amazonas, Apurímac, Huánuco, Madre de Dios, Pasco, and Tumbes, lacked any pathological anatomy services (236).

#### Lack of quality control in laboratories

• In Peru, a study published in 2015 found that 90% of 772 clinical laboratories (including public and private) were not conducting quality assurance. Quality assurance refers to a set of measures and procedures to ensure that the results of the tests and analyses conducted in a laboratory are reliable (232).

#### Lack of comprehensive biomarker testing

Table 6 provides an overview of biomarker tests in TNBC and their use in clinical practice. While tests for hormone receptor and HER2 status are routinely performed except in Mexico, tests for *BRCA* 1/2 mutations and PD-L1 status are not yet widely implemented.

Country	Tests for hormone receptor and HER2 status	Tests for <i>BRCA</i> 1/2 (with therapeutic intent)	Tests for PD-L1
<b>Argentina</b>	-Hormone receptor/HER2 status is routinely tested. However, HER2 testing usually takes longer for two reasons: (1) the payment for the HER2 test is dependent on the patient's health insurance, and (2) the clinician must request the test before pathologists can perform it.	-Tests are not reimbursed in the public sector. -Patient programs by pharmaceutical companies pay for testing in both the public and private sector.	-Tests are not reimbursed in the public sector. -Patient programs by pharmaceutical companies pay for testing in both the public and private sector.

#### Table 6: Availability of diagnostic tests for TNBC (2022/2023)



	- Hormone	-Coverage of comprehensive	Coverage of
Brazil	receptor/HER2 status are routinely done.	biomarker testing for BRCA status is limited in the public sector by a low coverage cap. -Patient programs pay for testing in both the public and private sector.	<ul> <li>Coverage of comprehensive biomarker testing for PD-L1 status is limited in the public sector by a low coverage cap.</li> <li>Patient programs pay for testing in both the public and private sector.</li> </ul>
* Chile	<ul> <li>-Hormone receptor/HER2 status is routinely tested and reimbursed.</li> <li>-The tests may not always happen upfront based on the biopsy, but rather after surgery based on the surgical sample.</li> </ul>	-Tests are not reimbursed in the public sector (160). -National clinical guidelines recommend patients with hereditary breast cancer to receive <i>BRCA</i> testing (235).	-PD-L1 test is not reimbursed. There is a basket for funding diagnostic breast cancer tests, but when oncologists need PD-L1 test results, there are generally no more funds left for additional tests.
Colombia	-They are recommended for all breast cancer patients. -In 2021, 89% of patients in the contributory system and 73% of patients in the subsidized system were tested for hormone receptors, and 86% and 70%, respectively for HER2 status (118).	-These tests are reimbursed in the public sector (237). However, access is limited by health care entities.	-These tests are reimbursed in the public sector (237). However, access is limited by health care entities.
Dominican Republic	- Hormone receptor/HER2 status are routinely done.	-Tests are not reimbursed in the public sector. -Patient programs by pharmaceutical companies pay for testing in both the public and private sector.	<ul> <li>These tests are typically done only in metastatic patients.</li> <li>Patient programs by pharmaceutical companies pay for testing in the public and private sector.</li> </ul>
Mexico	-They are considered a good practice (238). -The surgery can be carried out before the test results are available due to some surgeons' reluctance towards neoadjuvant systemic therapy.	<ul> <li>Tests are not reimbursed in the public sector.</li> <li>Patient support programs by pharmaceutical companies cover the test costs.</li> <li>National clinical guidelines only recommended testing in patients with a high risk of hereditary breast cancer and if "there are resources to conduct the test" (238).</li> </ul>	<ul> <li>-Tests are not reimbursed in the public sector.</li> <li>-Patient support programs by pharmaceutical companies cover the test costs.</li> <li>- National clinical guidelines make no mention of PD-L1 testing (238).</li> </ul>
Panama	- Hormone receptor/HER2 status are routinely done.	-Tests are reimbursed in the public sector.	-Tests are reimbursed in the public sector.



Peru	- Hormone receptor/ HER2 status testing are recognized as best practices, yet data on the percentage of biopsies undergoing these tests is currently	<ul> <li>Tests are not reimbursed in the public sector.</li> <li>Patient programs by pharmaceutical companies pay for testing in both the public and private sector.</li> </ul>	-Tests are not reimbursed in the public sector. -Patient programs by pharmaceutical companies pay for testing in both the public and
	these tests is currently unavailable.	public and private sector.	in both the public and private sector.

Notes: Information presented in the table comes from local experts unless otherwise cited. Data for Argentina, Brazil, Chile, and Mexico was collected in November 2022. For Colombia, the Dominican Republic, Panama, and Peru, the information was gathered in December 2023. Neoadjuvant therapy is the initial therapy for early-stage breast cancer and is carried out before surgery.

## 4.4 Challenges in treatment

The optimal treatment of TNBC differs by disease stage and tumor characteristics. A treatment plan should be drawn up by a multidisciplinary team (MDT), including at least a radiologist, radiographer, pathologist, breast surgeon, medical oncologist, radiation oncologist, breast care nurse, and breast data manager (147).

TNBC patients may be treated with surgery, radiation therapy, cancer medicines (systemic therapy), or a combination of these treatment modalities. Systemic therapy options in TNBC have historically been limited to chemotherapy (239). Since 2018, new options have become available globally with the introduction of immunotherapy and *BRCA* -targeted therapy in both early-stage and metastatic TNBC. Since 2022, international clinical guidelines by NCCN recommend these novel treatment options (108).

Figure 30 summarizes key challenges associated with the treatment of TNBC in the included Latin American countries. Note that not all challenges apply to every country.

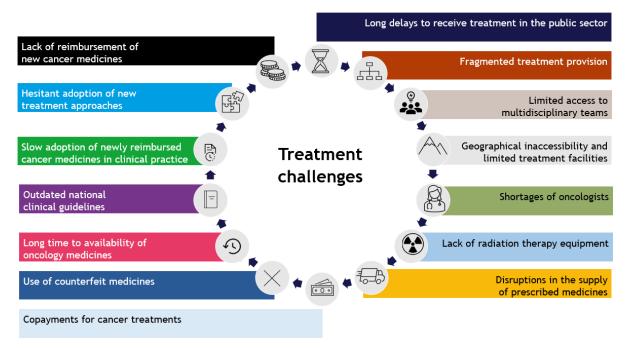


Figure 30: Challenges in the treatment of TNBC in Latin America.



#### Long delays to receive treatment

- In Chile, a law (GES, Explicit Health Guarantees) establishes that breast cancer treatment should start within 30 days of diagnostic confirmation (213). In a sample of patients diagnosed in 2017-2018, the mean time from diagnosis to surgery in patients without neoadjuvant systemic treatment (performed before surgery) was 66 days in the public sector and 30 days in the private sector (213).
- In Brazil, there were notable delays in initiating treatment following cancer diagnosis, leading the federal government to introduce the "Law of 60 days" in 2011 (240). This law aimed to set a maximum waiting period for cancer patients to receive treatment. However, a study revealed that the waiting times after the implementation of the law did not experience a noteworthy reduction compared with the time before (240).
- In Colombia, the average time between the first medical appointment and receiving chemotherapy is 100 days, and for breast surgery it is 120 days (199). Excessive paperwork to receive medical treatments has also been documented, as patients may need to reapply for medicines on a monthly basis or file legal claims to gain access to them once they are approved (199).
- In Argentina, according to a study from Buenos Aires, the average time to obtain surgery after a breast cancer diagnosis was approximately 50 days in the public sector, while in the private sector it was 18 days (241). Additionally, a significant difference in delays between the sectors was observed for receiving chemotherapy after surgery, with 83.5 days in the public sector and 48 days in the private sector.
- In Peru, during 2022, a total of 236 breast cancer surgeries were scheduled but remained unperformed, consequently accumulating in waiting lists at hospitals and specialized health institutes (242). This amounts to approximately 19% of the total cases treated within MINSA<sup>3</sup> (203). However, in 2023, national plans have been implemented to address the backlog of surgical interventions in public hospitals (242).
- In Peru, a survey conducted by the "Semaforo Oncologico" initiative, which involves 10 patient organizations dedicated to monitoring the implementation of the National Cancer Law, discovered that 65% of breast and cervix cancer patients had either delayed or halted their treatment (243). This delay was primarily attributed to challenges in securing timely medical appointments (42%). Additionally, 28% of the patients reported commencing their treatment three to five months after diagnosis (243).

#### Limited access to multidisciplinary teams

• The optimal management of TNBC patients requires expertise of different specialists to be discussed in multidisciplinary teams (MDT) as explained at the beginning of this section. A study found that there are challenges to access MDT in Latin America. According to a survey from this study, only 25% of researchers reported that participation in MDT is a mandatory component of breast cancer care in their countries, including Argentina, Brazil, Chile, and Peru (244). Other research has similarly identified this as a major obstacle in treating locally advanced breast cancer in the region (24). It also seems that patients with breast cancer receiving care in the private sector are more likely to be treated by MDT (24).



 $<sup>^{3}</sup>$  In 2022, there were 1237 breast cancer cases treated within MINSA

#### Fragmented treatment provision

- Receiving care from multiple institutions is associated with longer treatment times, higher health care costs, lower survival, and lower quality of life for patients in Latin America (245).
- In Colombia, cancer care is highly fragmented across multiple institutions, with patients receiving surgery, radiation therapy, and chemotherapy at different institutions. Referrals between institutions have been shown to predict all-cause mortality in breast cancer patients, with one additional referral being associated with a 27% increase in mortality (246).

#### Lack of information about and during treatment

• In a qualitative study in Peru, a majority of women stated that they lacked essential information throughout their entire treatment journey (158). This included information about the various treatment options available, expectations regarding their treatments, and potential side effects. Furthermore, the "Semaforo Oncologico" survey discovered that 46% of breast and cervix cancer patients surveyed were uncertain about the patient journey they should undertake after receiving their diagnosis (243).

#### Limited treatment facilities

- The National Oncology Institute (ION) is the only oncology hospital in Panama, and it has been reported that it works at its maximum capacity (247). There was a bidding process for the construction of a new hospital that was canceled in early 2023 due to lack of funds (247).
- In certain regions of Peru, like Tumbes, there is a significant deficiency in cancer care services, including essential resources like radiology and chemotherapy (203). As a result, cancer patients from this area are often referred to the Regional Institute of Neoplastic Diseases (IREN) in Trujillo, which is situated a daunting 700 kilometers away (203).

#### Geographical inaccessibility of treatment facilities

- A study conducted in 2014 shed light on the challenges faced by breast cancer patients residing in the provinces of Chiriqui, Herrera, Los Santos, and Veraguas (157). It revealed that a significant majority (75%) of these patients cited distance to the treatment center as their primary concern, while transportation to the facility posed a notable challenge for 49% of them (157). A 2022 project by Fundacáncer revealed that many patients require a combination of transport modes, including motorboats, buses, and taxis, to reach ION (248).
- In the 2023 survey conducted as part of the "Semaforo Oncologico" initiative mentioned earlier, it was revealed that 47% of breast and cervix cancer patients reported receiving treatment in a region different from their place of residence (243). They stated that half of the sample of breast and cervix cancer patients were required to travel to the capital city to access treatment (243).

#### Shortages of oncologists

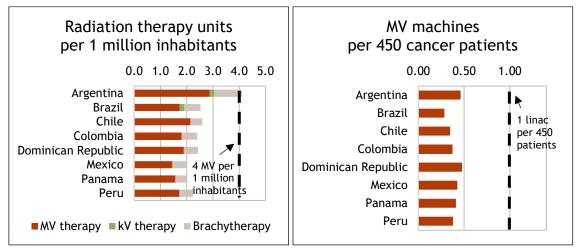
• In Colombia, there are only around 250 medical oncologists registered in the national oncology society (199), and even though the number of graduates is expected to

increase in the coming years, it will not be enough to make up for current shortages (249). The lack of medical oncologists can lead to long waiting lists or treatments provided by physicians that are not specialized in cancer treatment (250). In addition, most oncologists are concentrated in the most populated cities, leading to notable geographical disparities in access to treatment (199).

- In Panama, the field of oncology is one of the medical specialties with more pronounced shortages according to the Ministry of Health (161).
- In Peru in 2020, there were 319 medical oncologists affiliated with the Peruvian Society of Medical Oncologists (251). This translates into fewer than one medical oncologist per 100,000 inhabitants (0.99), while the United States had 3-4 per 100,000 inhabitants (251). Additionally, a significant majority of these oncologists are based in urban areas. Specifically, 73% of medical oncologists are located in Lima and Callao (236). In 2017, it was also noted that the vast majority (79%) of surgical oncologists were practicing exclusively in Lima and Callao (236).

#### Lack of radiation therapy equipment

• Most countries in this report have approximately 2.3 radiation therapy machines per 1 million inhabitants. Argentina stands out positively with 4.1 machines. To gauge whether these numbers meet the needs of the population, taking into account both current cancer patients and those who may develop the condition, the International Atomic Energy Agency (IAEA) has recommended a benchmark of 4 MV machines per 1 million inhabitants (252, 253). All countries in this study fall short of meeting this standard, as shown in Figure 31. Argentina has the highest number with 2.9 MV machines per 1 million inhabitants and Mexico the lowest number with 1.4 MV machines.



#### Figure 31: Radiation therapy units per inhabitants and per cancer patients in 2023.

Notes: MV = mega voltage, kV = kilo voltage. MV therapy includes medical linear accelerators (linacs) and cobalt-60 machines for external beam radiation therapy. Cancer patients refer to the estimated number of newly diagnosed cases in 2020 by the IARC. Data on radiation therapy units in the Dominican Republic refer to the year 2021. Source: DIRAC database (254).

• The IAEA and the European Society for Radiotherapy and Oncology (ESTRO) have put forth another recommendation that addresses the number of cancer patients requiring treatment. This recommendation is more closely aligned with the current demand, suggesting a target of one linear accelerator (MV machine) per 450 cancer patients



(255). No country currently reaches this benchmark as shown in Figure 31. The Dominican Republic and Argentina have the highest ratios, standing at 0.48 and 0.46, respectively, while Brazil boasts the lowest ratio, which is 0.28.

#### Disruptions in the supply of reimbursed medicines

- In Argentina, the Compulsory Medical Plan (Programa Médico Obligatorio) states that all cancer-related medicines should be provided for free to everyone covered with private insurances or by the national social security system. However, 70% of breast cancer patients receiving medical care in public facilities face disruptions in the provision of their medicines compared with only 11% of patients receiving care in private entities (98). Denials of or changes to prescribed medicines are not uncommon (256).
- In Peru, the 2023 survey carried out under the "Semaforo Oncologico" initiative showed that the second most frequent cause of treatment delays or disruptions for patients with breast and cervical cancer was due to issues with medication availability (243).
   10% of respondents who had experienced delays or had suspended their oncological treatment cited the absence of necessary medicines as the reason.
- Panama has experienced substantial price increases in cancer medicines, primarily because pharmacies do not directly purchase drugs from manufacturers but rather use intermediaries, leading to higher costs (257). According to a study on the price of medicines in the private sector, other reasons that explain the increase in prices is that the national pharmaceutical industry is estimated to produce only 6% of the required medications, and there is a lack of legal, fiscal, or economic incentives aimed at fostering domestic production (258).

#### Copayments for cancer treatments

In the Dominican Republic, the public healthcare system's coverage of cancer treatments and medical services is subject to copayments, which can restrict access for economically disadvantaged individuals. Healthcare coverage includes 80% of the expenses for medical consultations, surgeries, radiotherapy, and chemotherapy for critical conditions like breast cancer, along with 70% for outpatient medications (259) (260). Consequently, patients must contribute the remaining 20% and 30% of these costs (259). This financial strain intensifies once patients reach their coverage cap, necessitating them to shoulder all further expenses: see more in the challenge *limited reimbursement*. In 2022, the copayment was halved for serious illnesses (261). Nonetheless, concerns about the sustainability of this reduction emerged, as health insurance companies (ARS) were expected to absorb the other half(261). Private clinics have reported delays in these payments from ARS, leading to liquidity challenges (261).

#### Use of counterfeit medicines

Latin America is the second largest producer and marketer of counterfeit medicines according to the Institute of Research Against Counterfeit Medicines (262). Counterfeit medicines may put patients at serious risk because they lack active ingredients, contain incorrect doses of active ingredients, contain another active ingredient, etc.

• In Mexico, The Federal Commission for Protection against Health Risks (COFEPRIS) issued a warning in February 2022 that counterfeit lots of cancer immunotherapy were being distributed in the country (263).



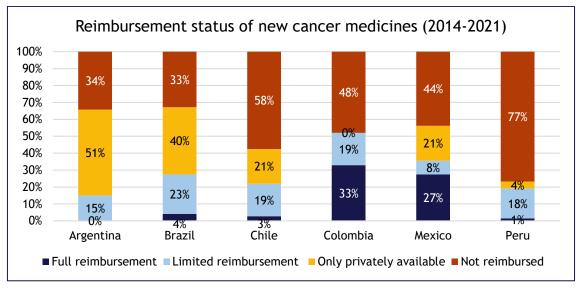
• In the Dominican Republic, the Special Prosecutor's Office for Crimes and Offenses Against Health (PEDECSA) has been collecting concerning data regarding the confiscation of pharmaceuticals and medical devices with uncertain origins (264). In 2017, it was estimated that illicit medicines, counterfeit, expired, relabeled, stolen, etc., accounted for approximately 10% of the entire private pharmaceutical market (265).

#### Outdated national clinical guidelines

- The Colombian clinical practice guidelines for early detection, treatment, monitoring, and rehabilitation of breast cancer were last updated in 2017. Medical treatments for metastatic TNBC only include chemotherapy (266), and no *BRCA* -targeted therapies or immunotherapies.
- In Peru, the 2019 version of the INEN's technical document on the disciplinary management of TNBC acknowledges advancements in targeted therapies, including developments in the field of immunotherapy (267). Despite this, such advancements have not been reflected in the treatment recommendations for either the early or advanced stages of the disease outlined in the document. Moreover, there have been no further updates to the document since 2019.

#### Limited reimbursement and long time to availability of new cancer medicines

• Patient access to newer cancer medicines is generally low in Latin America (268). The percentage of cancer medicines approved worldwide in 2014-2021 with full reimbursement by public payers in the selected countries in 2023 ranged from 0% to 33%, while 33% to 77% were not reimbursed in any way; see Figure 32. Low reimbursement rates are amongst other things linked to low public budgets for cancer medicines. For instance, the planned public budget allocated to innovative cancer medicines in Chile accounted for 12% of the total public budget for cancer care in 2022 (116). In comparison, spending on cancer medicines accounted for 31% of total cancer care expenditure in Europe in 2018 (95).



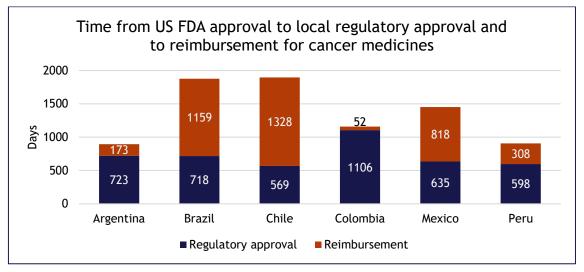
#### Figure 32: Reimbursement status of cancer medicines approved worldwide in 2014-2021.

Notes: The sample contains 73 cancer medicines with regulatory approval by the US FDA or the EMA received in 2014-2021. The category "not reimbursed" includes medicines with local regulatory approval



but no reimbursement, and medicines with no local regulatory approval. Source: FIFARMA Patients WAIT Indicator 2023 Latin America (268).

- In the Dominican Republic, the annual coverage cap for high-cost diseases, including medical appointments, surgeries, chemotherapy, radiotherapy, and medications, was set at a maximum of RD\$2,090,000 in 2022 (269). This increase increased from the previous limit of RD\$1,090,000, after numerous reports indicated the earlier amount was inadequate, often resulting in the halting of treatments (259, 270). This was particularly evident in advanced cancer cases, where some news outlets reported that patients exhausted their maximum coverage within four months while undergoing treatment (259). While the rise in the coverage limit is a step in the right direction, its adequacy remains to be evaluated.
- The mean time taken for oncology medicines to go from US FDA approval to local (full or limited) reimbursement in the studied countries was 3.7 years (271); see Figure 33. Data for Panama and the Dominican Republic were not available. Chile and Brazil experienced the longest wait times, with 5.2 and 5.1 years respectively. However, these numbers only reflect the duration experienced by medicines with eventual local reimbursement, whereas the duration for the many medicines that are not yet reimbursed (see Figure 32) might even be longer.
- Colombia took the longest to grant regulatory approval, averaging 3 years. This was followed by Argentina and Brazil, both taking 2 years on average.
- Considering the time between local regulatory approval and reimbursement, Chile and Brazil had the longest durations, with 3.6 and 3.2 years, respectively, whereas Colombia had the shortest duration with 52 days.



# Figure 33: Time from US FDA approval to local regulatory approval and reimbursement of cancer medicines approved worldwide in 2014-2020 on June 1<sup>st</sup>, 2022.

Notes: The sample differs in each country and only includes the subset of medicines with full or limited reimbursement out of the full sample 100 cancer medicines with global regulatory approval between 2014-2020. Source: FIFARMA Patients WAIT Indicator 2022 survey (271).

#### Slow adoption of newly reimbursed medicines and new treatment approaches

• In Mexico, the process of accessing new medicines in hospitals can be sluggish, even when medicines have received regulatory approval and reimbursement approval. Typically, it takes more than 5 years for cancer treatments to complete the journey



from regulatory approval to being added to the essential medicine lists in public institutions and becoming available in hospitals, whereas treatments for respiratory diseases only require 2.8 years (272). On average, hospitals take 1.6 years to adopt new cancer treatments, whereas new treatments for respiratory diseases and diabetes are adopted within 4 months and 6 months, respectively (272).

- In Colombia, reimbursement of new medicines is associated with the inclusion in the Health Benefits Plan (PBS) (273). However, delays in patients' access to new medicines in clinical practice are common, particularly in the subsidized regime. There are also significant budgetary constraints faced by public health care providers, making it difficult to provide access to newly reimbursed medicines to all eligible patients.
- Oncologists and surgeons may be reluctant to adopt new treatment regimens. An example is the neoadjuvant (performed before surgery) and adjuvant (performed after surgery) use of cancer medicines in TNBC patients who previously would not have received such treatments. Unpublished market research from 2021 showed that around 26% of non-metastatic TNBC patients in Brazil were taken directly to surgery without full assessment of their hormone receptor/HER2 status. Although there is limited data on the utilization of neoadjuvant systemic therapies in the studied countries, underutilization in this setting of breast cancer treatment has been reported in Europe and the United States (147, 274). A reluctancy to prescribe neoadjuvant systemic treatments to women with high-risk early-stage breast cancer by surgeons in Australia has also been report (275).





# 5. Societal impact of improved TNBC care

The previous chapter pointed to many opportunities to improve the care of TNBC patients in Latin America. The quality of care provided to patients determines not just their health outcomes but has wider implications for society. Figure 34 depicts different elements of the societal impact of TNBC. Apart from health outcomes, this includes effects on family life, the need for informal care, and work life, all of which have economic implications for patients, their families, and the economy.

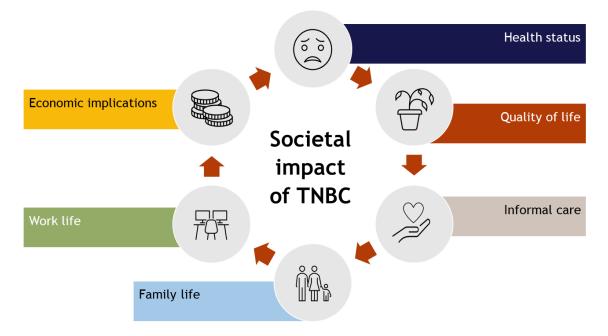


Figure 34: Elements of the societal impact of TNBC.

### Case: Improving early detection

Many women with breast cancer are diagnosed at advanced stages in Latin America. Improving the detection at earlier stages requires, amongst others, improvements in the (i) awareness of patients and primary health care workers about early signs and symptoms, and (ii) participation in screening programs of women in the target age group, (iii) implementation of organized population-based breast cancer screening programs in countries where they do not yet exist. The following effects of improved early detection may be anticipated:

- Health implications: The number of cancer survivors would increase. This is because more women are diagnosed at early stages and because the survival rates in TNBC are much higher in early stages than in late stages (e.g., 5-year survival rate of 92% in stage I but only 5% in stage IV in Peru (32); see section 3.2).
- Family life and informal care: The lower symptom burden of breast cancer in early stages than in late stages may reduce the amount of informal care required by patients. This may also positively affect family life. A diagnosis at an earlier stage may also lower the psychological burden on family members due to a reduced likelihood of losing a mother/spouse/partner.





- Work life: More women could continue to work during their initial treatment or resume work after it because of the lower symptom burden of breast cancer in early stages than in late stages.
- Economic implications: The treatment costs might decrease because the costs of treating TNBC are lower in the early stages than in the late stages. Indeed, in Latin America, annual per-patient medical costs for stage IV breast cancer are more than twice as high as for stage I (102); see section 3.3. The increased number of women surviving TNBC and being able to resume work also would reduce the indirect costs (productivity loss) to the economy.





# 6. Recommendations for improvement

The evidence gathered in this report shows that women with TNBC in Latin America face important challenges throughout their patient journey. Enhancing the timely provision of adequate care services to TNBC patients should be a priority. In many cases, this will require public investments. If these investments lead to better patient outcomes, there will be positive spillover effects to the economy. These spillover effects will likely be substantial because many TNBC patients are still of working age when they receive their diagnosis.

This report concludes with a list of recommendations to improve TNBC care in Latin America. These recommendations can be grouped into three main areas as shown in Figure 35. The implementation of these recommendations will require the cooperation of various stakeholders in each area. This includes foremost patient advocacy groups, the media, health care professionals (both in primary care and breast cancer specialists), hospitals and diagnostic centers, medical associations, and the Ministry of Health.

	Raise health literacy to facilitate early detection	
¢	Ensure optimal care delivery	
Ŵ	Consider adoption of innovation in clinical practice	

Figure 35: Main areas of improvement for TNBC care.

## Area 1: Raise health literacy to facilitate early detection

#### Improve breast cancer prevention

Around 20% of breast cancer cases in Latin America are potentially preventable because they are caused by modifiable risk factors, particularly obesity/overweight and physical inactivity. The promotion of a healthy diet and lifestyle is therefore important to avoid future incidences of breast cancer. Every cancer case avoided not only saves lives but also money for the health care system. However, cancer prevention is a long-term endeavor due to the considerable time lag between risk exposure and cancer development.

#### Raise awareness of breast cancer symptoms

Adult women of all ages have a great responsibility to be aware of early signs and symptoms of breast cancer. This is especially important in Latin America due to the lack of effective screening programs. The promotion of breast health awareness needs to be prioritized.



#### Enhance involvement of primary care in early detection

Primary care can play a crucial role in improving outcomes for breast cancer patients. This requires better training of primary care workers in early breast cancer detection. Primary care workers should also actively promote participation in screening among the women they treat. Swift referral pathways from primary care to diagnostic services need to be established or strengthened.

#### Personalize risk assessment through BRCA genetic testing

Many women with *BRCA* 1/2 mutations are unaware they have them. Offering genetic testing/counseling to women who are at an increased risk of developing TNBC (such as women with a family history of breast or ovarian cancer) can potentially increase the chances of early diagnosis, as those with increased genetic risk will pay close attention to early symptoms of breast cancer.

#### Promote participation in screening programs

All Latin American countries (with the exception of Chile) have comparatively low participation rates of only around 10-30% in breast cancer screening programs. Raising women's knowledge and understanding of the potential benefits and harms of participating in screening programs is critical for enhancing early detection.

## Area 2: Ensure optimal care delivery

#### Address the underfunding and fragmentation of health care systems

A fundamental challenge for breast cancer patients in Latin America are underfunded and fragmented health systems. This fragmentation, along with the coexistence of multiple insurance programs that cater to different socioeconomic groups with varying funds and benefits, exacerbates inequalities in access to health care. The dependence on the private sector, coupled with the insufficient effective coverage provided by the public sector, leads to out-of-pocket expenses that disproportionately burden lower socioeconomic groups with limited financial resources, further perpetuating these inequalities. The growing demand for health care due to population aging will add additional pressure on the health care systems. The provision of effective and cost-effective health care, including breast cancer care, should therefore be a priority.

#### Overhaul national breast screening programs

Although many countries offer subsidized or free mammography screenings for a certain target population, the screening programs are opportunistic and often fragmented rather than being part of an organized and unified national strategy. As a result, only about 10% to 30% of the target population undergoes mammography screenings (Chile is an exception to this trend). Many reasons for these low screening rates have been identified. These include (i) lack of organized population-based programs with individualized invitations, (ii) lack of awareness of the benefits of screening, (iii) low number of mammography machines, (iv) uneven geographical distribution of mammography machines, (v) lack of clarity about which screening facility to attend, (vi) long waiting lists to get a screening appointment, (vii) low perceived quality of screening services in the public sector. This long list of barriers calls for a major overhaul of the current screening programs. In addition, countries that still have screening programs with





a narrow target group (e.g., women aged 50-69 years) could consider broadening the target group to 50-74 years, in line with the 1<sup>st</sup> edition of the Latin America and the Caribbean Code Against Cancer issued by IARC and PAHO in 2023, or to 45-74 years in line with the latest recommendation from the Council of the European Union. The expansion to younger ages would especially help to detect more cases of TNBC earlier.

#### Establish clear care pathways

Long delays between diagnosis and start of treatment are common in the public sector in Latin American countries. These delays decrease the chances of positive treatment outcomes. The delays are caused by a multitude of factors, including shortages of physicians involved in the diagnostic process (radiologists, pathologists) and in treatment (surgeons, medical oncologists, radiologists), lack of diagnostic infrastructure, and fragmentation of diagnostic services and treatment services. The establishment of clear patient pathways, starting from suspicion of breast cancer in primary care (or from mammography screening) through treatment start should be prioritized. This will help to improve the coordination between primary, secondary, and tertiary health care providers.

#### Assure high quality of breast cancer imaging

The use of old mammography machines leads to a high proportion of inconclusive tests and diminishes efforts in breast cancer screening across Latin American countries. Low quality of mammograms leads to poor accuracy of clinical diagnosis, necessitating repeated tests, causing delays in early detection, and raising costs in the long run. Quality control procedures should be implemented to ensure that breast cancer imaging operates correctly. This includes proper selection of imaging technology, prompt detection of deviations from optimal performance, and the training of radiologists.

# Ensure a swift and complete pathological assessment before treatment start

In Latin America, basic biomarker testing might not be carried out in all early-stage breast cancer patients prior to surgery, thus limiting the use of neoadjuvant systemic therapy (performed before surgery). A full assessment of staging and ER/PR/HER2 status should be completed before the start of treatment in order to enable the choice of the most suitable therapeutic approach. At the same time, the pathological assessment should not unnecessarily delay the start of treatment. Small and general pathology laboratories could be consolidated into larger conglomerates to achieve a sufficient volume of cases. This would facilitate the adoption of national and international best practices and enable specialization of pathologists in specific disease areas, including breast pathology. Quality assurance schemes should be put in place in all pathology laboratories.

#### Recruit and train pathologists, oncologists, and radiologists

There are distinct shortages of pathologists, oncologist, and radiologists in Latin American countries. This creates long turnaround times in the diagnostic process and may limit the services to be received. As the number of breast cancer patients is expected to rise further in the coming decades, the recruitment and training of these specialized physicians should be prioritized.





There are challenges for breast cancer patients to access MDTs in Latin America. This has already been identified as one of the main obstacles for treating locally advanced breast cancer in the region. TNBC necessitates more complex treatment decisions that can benefit from the diverse expertise present in an MDT. MDTs are collectively usually more informed about the latest research, clinical trials, and emerging treatment options, which can be beneficial for TNBC patients. Finally, the diagnosis of TNBC can be particularly challenging for patients due to its aggressive nature and the complexities involved in its treatment. MDTs often include or have access to psychosocial support and can address the broader needs of patients and their families, providing comprehensive care.

#### Ensure timely availability and utilization of prescribed medicines

Even if new treatments have regulatory approval and are covered by insurance, there are often bottlenecks in the supply of cancer medicines. These bottlenecks can be caused by various factors, such as underfunding or supply chain management issues. As a result, not all patients may have reliable access to effective treatments, and they may experience interruptions in their treatment. To ensure that all eligible patients have access to their prescribed treatments, it is essential to prioritize adequate public funding for hospitals and health care systems so they can purchase and stock the medicines. Additionally, improving supply chain management can help to minimize the risk of stockouts and ensure that treatments are readily available to patients when needed.

## Area 3: Consider adoption of innovation in clinical practice

#### Expand access to comprehensive biomarker testing

Testing for *BRCA* 1/2 mutations in both early-stage and metastatic TNBC and testing for PD-L1 expression in metastatic TNBC are required prior to the administration of modern cancer medicines. Patient access to these tests needs to be guaranteed to enable the choice of the most appropriate and effective therapeutic approach. Adequate testing infrastructure also needs to be put in place. Currently, these tests are not fully covered in the public sector across all Latin American countries. Tests are typically accessible only through special patient access programs or are paid for by patients out-of-pocket.

#### Enhance regulatory efficiency

The delay in the approval of innovative treatments means that TNBC patients may miss out on advanced therapies that could improve their survival rates and quality of life. TNBC tends to progress faster than other types of breast cancer. Any delay in accessing the most effective treatments can cause disease progression, making the cancer more difficult to treat and having a significant impact on patient outcomes. Also, waiting for new treatments can be emotionally draining for patients and their families.

#### Take steps to expand access to appropriate medicines in the public sector

The availability of modern cancer medicines is generally low in Latin American countries, as many medicines are not reimbursed by public payers. Access to these medicines is limited to patients with comprehensive private insurance seeking treatment in the private sector and to those with substantial private financial resources to pay out-of-pocket. It is crucial for public



payers to consider the reimbursement of cancer medicines that offer significant clinical benefits. The availability of new effective medicines could potentially alleviate other components of the economic burden associated with TNBC, such as productivity loss and informal care.

#### Update local clinical guidelines

Since 2018, new treatment options for TNBC have emerged and have already been included in international clinical guidelines. It is essential for local guidelines to be promptly updated whenever new diagnostic tests and treatments become available in the local setting. This will facilitate the selection of appropriate treatment options in the rapidly evolving and complex landscape of TNBC treatment.

#### Update care pathways and provide training to clinical staff

The introduction of novel treatment options requires some adaptations of the care pathway, e.g., because more patient groups are recommended to receive neoadjuvant (performed before surgery) and/or adjuvant (performed after surgery) therapy with cancer medicines. To ensure the optimal utilization of these novel treatment options, clinical staff, including pathologists, breast surgeons, medical oncologists, radiation oncologists, and others, must receive appropriate training.



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## Annex – Country cards







Brazil

Population: 215.3 million (2022) GDP per capita: USD 8,918 (2022) Life expectancy: 73 years (2021) Total health expenditure: 9.9% of GDP (2021) Source: World Bank

Triple-Negative Breast Cancer (TNBC)		
<ul> <li>Breast cancer is the most common cancer type in women (32% of all new cancer cases) and responsil</li> <li>Around 21% of new breast cancer cases are of the TNBC subtype.</li> <li>TNBC is more aggressive than other breast cancer subtypes. It tends to affect younger women, is ty</li> </ul>	pically diagnosed later in more advanced	
clinical stages, has higher chances of recurrence after initial treatment, and has one of the lowest su Health system readiness	urvival rates of all breast cancer subtypes.	
Challenges	Recommendations	
<ul> <li>Inadequate health care access despite universal health coverage. According to the WHO, the average coverage of essential health care services is only 75 points out of 100, lower than in Colombia and Chile (78 and 80, respectively). This indicates that a significant portion of the demand for essential health care remains unmet.</li> <li>Inequities in access to care in the public vs. the private sector. 75% of the population is covered by the public insurance and 25% by private insurances. Publicly insured patients face longer delays in accessing virtually all health care services. For instance, in the public sector, 40% of breast cancer cases are diagnosed late in advanced clinical stages, compared to only 16% in the private sector.</li> <li>The fragmented health care system with a high reliance on the private sector impedes national efforts for breast cancer prevention and control programs.</li> <li>More than 25% of the female population is obese and over 50% of women are not sufficiently physically active, which increases the risk to get breast cancer. An estimated 10% of breast cancer cases could theoretically be preventable in the absence of obesity/overweight and a further 4% with more physical activity.</li> </ul>	<ul> <li>Continue the development of the health system to achieve better coverage of all essential health care services to the entire population.</li> <li>Strive for a more equitable distribution in the provision of health care services between the public and the private sector.</li> <li>Create effective national prevention strategies to halt rising levels in obesity and physical inactivity.</li> </ul>	
Early detection		
Challenges	Recommendations	
<ul> <li>A shortage of primary care physicians contributes to long wait times for health care in some areas. This leads to delays in the early diagnosis of women with breast cancer symptoms.</li> <li>The national breast cancer screening program for women aged 50-69 only achieves a participation rate of 32% in women aged 50-59 and 25% in women aged 60-69. This is despite the screening being free for the target population. Low participation partly explains why around 40% of breast cancer diagnoses are made at an advanced clinical stage.</li> <li>The organization of the screening program is inadequate. Eligible women for screening are not systematically identified and invited.</li> <li>Insufficient mammography equipment coverage, primarily in the North and Northeast.</li> <li>Many mammography machines operate at inadequate levels of quality, increasing the risk of incorrect diagnosis.</li> <li>Due to COVID-19 control measures, disruptions in the cancer screening program and changes in patient behavior have led to reductions in screening.</li> </ul>	<ul> <li>Strengthen the role of primary care in early detection of breast cancer.</li> <li>Run public campaigns to increase participation in the breast screening program.</li> <li>Implement fixed appointments and reminders for the breast cancer screening program.</li> <li>Improve geographical access to mammography screening.</li> <li>Prioritize quality assurance and quality control of mammography machines.</li> <li>Intensify efforts to boost participation in breast cancer screening in the aftermath of the COVID-19 pandemic.</li> </ul>	
Diagnostic services		
Challenges	Recommendations	
<ul> <li>There is a shortage of specialists involved in the imaging of breast cancer, which leads to delays in the diagnostic process.</li> <li>There is a critical shortage of pathology laboratories in many hospitals, which forces samples to be transported to external laboratories. This creates numerous opportunities for quality failures, leading to a need for re-biopsy if the tissue sample gets impaired.</li> <li>Coverage of comprehensive biomarker testing for <i>BRCA</i> and PD-L1 status is limited in the public sector by a low coverage cap. Either patients pay for the tests out-of-pocket or through patient support programs</li> </ul>	<ul> <li>Invest in recruitment and skills of health care professionals in breast imaging.</li> <li>Consolidate diagnostic services and ensure safe transportation of samples to external laboratories.</li> <li>Expand access to biomarker testing for <i>BRCA</i> and PD-L1 status.</li> </ul>	
Treatment	Decementations	
<ul> <li>Challenges</li> <li>Limited access to appropriate cancer care in the public sector. The FIFARMA Patients WAIT Indicator 2023 survey indicated that only 4% of patients in the public sector have full access to cancer medicines launched globally in 2014-2021.</li> </ul>	<ul> <li>Enhance patient access to cancer medicines in the public sector.</li> </ul>	

* Chile	Population: 19.6 million (2022) GDP per capita: USD 15,356 (2022) Life expectancy: 79 years (2021) Total health expenditure: 9.3% of GDP (2021) Source: World Bank	
Triple-Negative Breast Cancer (TNBC)		
<ul> <li>Breast cancer is the most common cancer type in women (22% of all new cancer cases) and responsi</li> <li>Around 11-14% of new breast cancer cases are of the TNBC subtype.</li> </ul>		
• TNBC is more aggressive than other breast cancer subtypes. It tends to affect younger women, is ty clinical stages, has higher chances of recurrence after initial treatment, and has one of the lowest subtypes.		
Health system readiness		
Challenges	Recommendations	
<ul> <li>Inequities in access to care in the public vs. the private sector. 78% of the population is covered by public insurance (Fonasa) and 17% by private insurances (Isapre). There are differences in the eligibility criteria for public and private health coverage, mainly divided by level of health risks and income levels. Breast cancer patients in the public sector are more likely to be diagnosed at advanced stages and must wait longer for treatment initiation than in the private sector.</li> <li>Public spending on cancer care accounts for 3% of the total health care budget, which is less than half of what many countries in Europe spend on cancer care.</li> <li>More than 30% of the female population is obese and almost 30% of women are not sufficiently physically active, which increases the risk to get breast cancer.</li> </ul>	<ul> <li>Strive for a more equitable coverage of health care services across the public and private health care regimes.</li> <li>Increase public funding of cancer care.</li> <li>Create effective national prevention strategies to halt rising levels in obesity and physical inactivity.</li> </ul>	
Early detection		
Challenges	Recommendations	
<ul> <li>A shortage of primary care physicians contributes to long wait times for health care in some areas. There is also a lack of early detection training for breast cancer of primary health workers in public facilities. This leads to delays in the early diagnosis of women with breast cancer symptoms.</li> <li>Early detection of breast cancer is partly hampered by patient preferences and behavior. Many women still prefer self-detection. In addition, certain breast cancer signs are not widely known, so women might risk delaying their diagnosis if they do not go to a medical checkup.</li> <li>The national breast cancer screening program aimed at women aged 50 to 59 (previously 50-69 years) achieves a self-reported participation rate of over 70%, a high figure compared to other countries in the region. However, there are significant disparities across socioeconomic groups, with a screening rate of only 34% in low socioeconomic groups. This relates partly to inadequate information-sharing strategies to address low socioeconomic groups.</li> <li>Even though a medical order is not required today, women rely on the advice of primary care health professionals to get a mammogram.</li> <li>The public sector lacks sufficient mammography machines, often leading to outsourcing to the private sector. Incentives typically favor the least expensive offers, which often have the lowest quality standards.</li> <li>A significant number of mammograms yield inconclusive results. In Santiago alone, some studies show this figure rising to 23%, reflecting potential quality deficiencies and leading to higher costs due to the need to repeat the tests.</li> <li>Due to COVID-19 control measures, disruptions in the cancer screening program and changes in patient behavior have led to reductions in screening.</li> <li>In primary care, there is a high turnover of health professionals.</li> </ul>	<ul> <li>Strengthen the role of primary care in early detection of breast cancer.</li> <li>Raise awareness of breast cancer symptoms among women.</li> <li>Improve information-sharing strategies about screening to low socioeconomic groups.</li> <li>Prioritize quality assurance and quality control of mammography machines in the public and private sector.</li> <li>Intensify efforts to boost participation in breast cancer screening in the aftermath of the COVID-19 pandemic.</li> <li>Develop continuing medical education plans for health professionals in primary care.</li> </ul>	
Diagnostic services		
<ul> <li>Challenges</li> <li>Poor coordination between primary and secondary care impedes timely referrals. This leads to long waiting times and delays in the early diagnosis of women with breast cancer symptoms.</li> <li>There is a shortage of infrastructure for pathology services, and a lack of training in pathology courses and few possibilities for internships in breast pathology units.</li> <li>Hormone receptor/HER2 status tests are performed routinely, but they are not always performed upfront based on the biopsy sample. In some cases, these tests might only be performed after surgery based on the surgical sample, which limits the choice of the most appropriate treatment approach such as neoadjuvant systemic therapy (performed before surgery).</li> <li>Comprehensive biomarker testing for <i>BRCA</i> and PD-L1 status is not covered in the public sector. Either patients need to pay for the tests out-of-pocket or pharmaceutical companies cover them through patient support programs.</li> <li>Limited access to appropriate cancer care in the public sector. The FIFARMA Patients WAIT Indicator 2023 survey indicated that patients in the public sector only have full access to 3% of all cancer medicines launched globally in 2014-2021.</li> </ul>	<ul> <li>Recommendations</li> <li>Establish clear and rapid care pathways for breast cancer patients in the public sector.</li> <li>Prioritize investment in pathology services and training of pathologists.</li> <li>Ensure that all women are tested upfront for hormone receptor/HER2 status.</li> <li>Expand access to biomarker testing for <i>BRCA</i> and PD-L1 status.</li> <li>Enhance patient access to cancer medicines in the public sector.</li> <li>Address the disparity in TNBC, as it represents the only group of breast cancer patients without access to new treatments.</li> </ul>	



Population: 51.9 million (2022) GDP per capita: USD 6,630 (2022) Life expectancy: 73 years (2021) Total health expenditure: 9.0% of GDP (2021) Source: World Bank

Triple-Negative Breast Cancer (TNBC)				
<ul> <li>Breast cancer is the most common cancer type in women (28% of all new cancer cases) and responsi</li> <li>Around 15% of new breast cancer cases are of the TNBC subtype.</li> </ul>	ble for 17% of all female cancer deaths.			
<ul> <li>TNBC is more aggressive than other breast cancer subtypes. It tends to affect younger women, is typically diagnosed later in more advanced clinical stages, has higher chances of recurrence after initial treatment, and has one of the lowest survival rates of all breast cancer subtypes.</li> </ul>				
Health system readiness	arrivat rates of all breast cancer subtypes.			
Challenges	Recommendations			
<ul> <li>Inadequate health care access despite universal health coverage. According to the WHO, the average coverage of essential health care services is 78 points out of 100, lower than in Chile (80 points). This indicates that a significant portion of the demand for essential health care remains unmet.</li> <li>Inequities in access to care in the public sector. The public system is divided into a contributive regime (45% of the population) and a subsidized regime (49%). Breast cancer patients in the subsidized regime face greater challenges throughout their patient journey, including longer delays and poorer access to services.</li> <li>The fragmented health care system impedes national efforts for breast cancer prevention and control programs.</li> <li>More than 25% of the female population is obese and almost 50% of women are not sufficiently physically active, which increases the risk to get breast cancer.</li> </ul>	<ul> <li>Strengthen the provision of essential health care services in the public sector overall.</li> <li>Strive for a more equitable coverage of health care services, with a focus on the subsidized regime.</li> <li>Create effective national prevention strategies to halt rising levels in obesity and physical inactivity.</li> </ul>			
Early detection Challenges	Recommendations			
<ul> <li>Early detection of breast cancer is partially hindered by patients' preferences and context. Many women still prefer self-examination and are unaware that mammography is the most effective method for early detection. Furthermore, the lack of knowledge about certain signs of breast cancer could lead to delays in diagnosis if they do not seek a medical check-up.</li> <li>The national breast cancer screening program for women aged 50-69 only achieves a participation rate of close to 30%, with significant disparities across regions. Low participation partly explains why around 33% of breast cancer diagnoses are made at an advanced clinical stage.</li> <li>A large proportion of women rely on the advice of their primary care physician to get a mammogram, which indicates a failure of screening programs to entice women to attend breast screening out of</li> </ul>	<ul> <li>Raise awareness of breast cancer symptoms among women.</li> <li>Run public campaigns to increase participation in the breast screening program.</li> <li>Implement fixed appointments and reminders for the breast cancer screening program, including information about which clinic to</li> </ul>			
<ul> <li>habit.</li> <li>Women must wait a long time to schedule appointments for breast cancer screenings.</li> <li>Unclear public information about which medical facility women should visit to get screened.</li> <li>Despite the screening program being for free, many women still opt to pay for mammograms in the private sector due to quality concerns.</li> </ul>	<ul> <li>Increase the availability of mammography machines to reduce waiting times.</li> <li>Prioritize quality assurance and quality control of mammography machines.</li> </ul>			
Diagnostic services				
<ul> <li>Challenges</li> <li>There is a shortage of pathologists, leading to delays in diagnosis. This leads to long waiting times and delays in the early diagnosis of women with breast cancer symptoms.</li> <li>Tests for hormone receptor status and HER2 status are recommended in the public sector, but patients in the subsidized regime get significantly fewer tests than patients in the contributory system.</li> </ul>	<ul> <li>Recommendations</li> <li>Invest in recruitment and training of pathologists.</li> <li>Ensure upfront testing for hormone receptor/ HER2 status for all patients by default.</li> <li>Continue ensuring access to biomarker testing for BRCA and PD-L1 status.</li> </ul>			
Treatment				
Challenges	Recommendations			
<ul> <li>Patients may receive care from multiple institutions due to the high fragmentation of the health system, which often leads to delays and ultimately impairs survival chances.</li> <li>There is a shortage of medical oncologists.</li> <li>There is excessive paperwork involved in receiving certain medical treatments, as patients may need to reapply for medicines on a monthly basis or file legal claims to gain access to them once they are approved.</li> <li>Budget constraints of public health care providers make it difficult to provide access to newly reimbursed medicines to all eligible patients, particularly in the subsidized regime.</li> <li>There is a lack of patient access to new cancer medicines. The FIFARMA Patients WAIT Indicator 2023 survey indicated that patients in the public sector only have full access to 33% of all cancer medicines launched globally in 2014-2021.</li> <li>Outdated national clinical guidelines for breast cancer treatment from 2017.</li> </ul>	<ul> <li>Improve the coordination between different cancer care service providers.</li> <li>Invest in recruitment and training of medical oncologists.</li> <li>Improve the bureaucracy to ensure patients can receive prescribed medicines.</li> <li>Enhance patient access to cancer medicines in the public sector.</li> <li>Update national clinical guidelines for TNBC.</li> </ul>			



## **Dominican Republic**

Population: 11.2 million (2022) GDP per capita: USD 10,120 (2022) Life expectancy: 73 years (2021) Total health expenditure: 4.9% of GDP (2021) Source: World Bank

Triple-Negative Breast Cancer (TNBC)	
Breast cancer is the most common cancer type in women (35% of all new cancer cases) and respons	ible for 26% of all female cancer deaths.
Around 13-21% of new breast cancer cases are of the TNBC subtype in Latin America.	
<ul> <li>TNBC is more aggressive than other breast cancer subtypes. It tends to affect younger women, is t</li> </ul>	
clinical stages, has higher chances of recurrence after initial treatment, and has one of the lowest s	survival rates of all breast cancer subtypes
Health system readiness	
Challenges	Recommendations
<ul> <li>Inadequate health care access despite universal health coverage. According to the WHO, the average coverage of essential health care services is only 66 points out of 100, lower than in Argentina, Mexico, Brazil, Panama, Colombia, Peru, and Chile (73, 74, 75, 77, 78, 78, and 80, respectively). This indicates that a significant portion of the demand for essential health care remains unmet.</li> <li>Low public funding of health care. Public health expenditure accounts only for around 3% of GDP, lower than comparable countries in Latin America and below the informal WHO target of 5%.</li> <li>Approximately 34% of women are obese, and about 43% are not engaging in sufficient physical activity, both of which elevate the risk of breast cancer.</li> </ul>	<ul> <li>Continue the development of the health system to achieve better coverage of all essential health care services to the entire population.</li> <li>Increase public investment in health care in line with comparable countries.</li> <li>Create effective national prevention strategies to halt rising levels in obesity and physical inactivity.</li> </ul>
Early detection	
Challenges	Recommendations
• A shortage of primary care physicians and nurses contributes to long wait times for health care in some areas. With roughly just one physician and one nurse (or midwife) for every 1,000	<ul> <li>Increase the number of seats in medical and nursing schools.</li> <li>Improve health service provision in underserved areas.</li> <li>Continue expanding the "Early Detection Program".</li> </ul>
<ul> <li>cancer.</li> <li>Recent initiatives, like the "Early Detection Program", aim to enhance breast cancer screening. While participation rates in this program are not available, it is inferred that they remain low because approximately 60% of breast cancer diagnoses occur at advanced clinical stages (stage III and IV). In addition, the program is only available in 10 hospitals and does not cover the whole country.</li> <li>Mammography units for screening activities are not accredited, which may compromise the quality of the results.</li> </ul>	<ul> <li>Establish KPIs for the breast cancer screening program, monitor their progress, and make them publicly accessible.</li> <li>Implement fixed appointments and reminders for the breast cancer screening program.</li> <li>Prioritize quality assurance and quality control of mammography units.</li> </ul>
Diagnostic services	
Challenges	Recommendations
• Comprehensive biomarker testing for <i>BRCA</i> and PD-L1 are not covered in the public sector. Either patients need to pay for the tests out-of-pocket or pharmaceutical companies cover them through patient support programs.	• Expand access to biomarker testing for <i>BRCA</i> and PD-L1.
Treatment	
Challenges	Recommendations
	<ul> <li>Increase the availability of radiation therapy and explore the use of hypofractionation.</li> <li>Strengthen legislation and action to combat the use of counterfeit medicines.</li> <li>Assess the effectiveness of the implemented reduction in copayment rates and the new annual coverage cap.</li> </ul>



## Mexico

Population: 127.5 million (2022) GDP per capita: USD 11,091 (2022) Life expectancy: 70 years (2021) Total health expenditure: 6.1% of GDP (2021) Source: World Bank

	Triple-Negative Breast Cancer (TNBC)						
•	Breast cancer is the most common cancer type in women (29% of all new cancer cases) and responsi Around 14% of new breast cancer cases are of the TNBC subtype.						
•	<ul> <li>TNBC is more aggressive than other breast cancer subtypes. It tends to affect younger women, is typically diagnosed later in more advanced clinical stages, has higher chances of recurrence after initial treatment, and has one of the lowest survival rates of all breast cancer subtypes.</li> </ul>						
	Health system readiness						
Cha	allenges	Re	commendations				
•	Inadequate health care access despite universal health coverage. According to the WHO, the average coverage of essential health care services is only 74 points out of 100, lower than in Brazil, Colombia, and Chile (75, 78 and 80, respectively). This indicates that a significant portion of the demand for essential health care remains unmet. Low public funding of health care. Public health expenditure accounts only for around 3% of GDP, lower than comparable countries in Latin America and below the informal WHO target of 5%. Inequities in access to care in the public vs. the private sector. 83% of women in the public sector are diagnosed with breast cancer based on symptoms instead of being asymptomatically diagnosed through screening, compared to 48% in the private sector. Also, 31% of breast cancer patients treated in the public sector were diagnosed at a late clinical stage, compared to 18% in the private sector. Public under-investment in initiatives to promote health and prevent breast cancer. More than 30% of the female population is obese and more than 30% of women are not sufficiently physically active, which increases the risk to get breast cancer.	•	Continue the development of the health system to achieve better coverage of all essential health care services to the entire population. Increase public investment in health care in line with comparable countries. Strive for a more equitable distribution in the provision of health care services between the multiple coverage schemes. Create effective national prevention strategies to halt rising levels in obesity and physical				
	Carly detection		inactivity.				
Ch	Early detection allenges	Re	ecommendations				
•	Early detection of breast cancer is partly hampered by patient preferences and behavior. Many women still prefer self-detection, and do not know or understand that mammography is the most effective method for early detection. In addition, certain breast cancer signs are not widely known, so women might risk delaying their diagnosis if they do not go to a medical checkup. Young women with symptoms might not be promptly referred from primary care to diagnostic services because primary care workers do not suspect breast cancer. There is no single nationwide population-based breast screening program. Women aged 40-69 are only encouraged to get screened, but the responsibility falls on them. This leads to low screening rates of around 15-25% in the target population. Low participation partly explains why the majority of breast cancer diagnoses are made at an advanced clinical stage. A large proportion of women rely on the advice of their primary care physician to get a mammogram. There is a high shortage of mammography machines. The uptake of screening is lower in rural and semi-urban communities due to geographic barriers and social determinants of health in comparison to urban areas. Due to COVID-19 control measures, disruptions in the cancer screening program and changes in patient behavior have led to reductions in screening.	•	Raise awareness of breast cancer symptoms among women. Train primary care workers in the early detection of breast cancer. Implement a national organized population-based breast cancer screening program. Improve the availability of mammography machines overall and in particular in rural areas. Intensify efforts to boost participation in breast cancer screening in the aftermath of the COVID-19 pandemic.				
	Diagnostic services						
Chi	Allenges There is a lack of clear referral routes for women with breast cancer symptoms receiving care in the public system. There is a general shortage of radiologists, and particularly radiologists specialized in breast imaging, which leads to delays in the diagnostic process. Long waiting times in diagnostic services push women to get tested in private facilities, sometimes in places that do not fulfill quality standards. When women return to public facilities for treatment, they often must re-do tests. Testing for hormone receptor status and HER2 status is recommended, but they are not always performed upfront based on the biopsy sample. In some cases, these tests might only be performed after surgery based on the surgical sample, which limits the choice of the most appropriate treatment approach such as neoadjuvant systemic therapy (performed before surgery). Some surgeons may also be reluctant of neoadjuvant systemic therapy. Comprehensive biomarker testing for <i>BRCA</i> and PD-L1 status is not covered in the public sector. Either patients need to pay for the tests out-of-pocket or pharmaceutical companies cover them through patient support programs. <b>Treatment</b>	•	Establish clear and rapid care pathways for breast cancer patients in the public sector. Prioritize recruitment and training of radiologists specialized in breast imaging. Ensure that all women are tested upfront for hormone receptor/HER2 status, and that the test results are used to inform the treatment decision. Expand access to biomarker testing for <i>BRCA</i> and PD-L1 status.				
Ch	allenges	Re	ecommendations				
•	Patient access to newly reimbursed medicines in public hospitals can be sluggish due to slow adoption. Limited access to appropriate cancer care in the public sector. The FIFARMA Patients WAIT Indicator 2023 survey indicated that patients in the public sector only have full access to 27% of all cancer medicines launched globally in 2014-2021. Use of counterfeit medicines puts patients at serious risk.	•	Enhance patient access to cancer medicines in the public sector. Strengthen legislation to combat the use of counterfeit medicines.				

THE



## Panama

Population: 4.4 million (2022) GDP per capita: USD 17,357 (2022) Life expectancy: 76 years (2021) Total health expenditure: 9.7% of GDP (2021) Source: World Bank

Triple-Negative Breast Cancer (TNBC)						
• Breast cancer is the most common cancer type in women (27% of all new cancer cases) and responsible for 17% of all female cancer deaths.						
Around 13-21% of new breast cancer cases are of the TNBC subtype in Latin America.						
• TNBC is more aggressive than other breast cancer subtypes. It tends to affect younger women, is typically diagnosed later in more advanced						
clinical stages, has higher chances of recurrence after initial treatment, and has one of the lowest survival rates of all breast cancer subtypes.						
Health system readiness						
Challenges	Recommendations					
<ul> <li>Inadequate health care access despite universal health coverage. According to the WHO, the average coverage of essential health care services is 77 points out of 100, lower than in Colombia, Peru, and Chile (78, 78, and 80 points, respectively). This indicates that a significant portion of the demand for essential health care remains unmet.</li> <li>Around 28% of the female population is obese and 65% of women are not sufficiently physically active, which increases the risk to get breast cancer.</li> </ul>	<ul> <li>Strengthen the provision of essential health care services in the public sector overall.</li> <li>Create effective national prevention strategies to halt rising levels in obesity and physical inactivity.</li> </ul>					
Challenges	Recommendations					
<ul> <li>Early detection of breast cancer is partially hindered by patients' preferences and context. Due to limited awareness, many women mistakenly view a breast cancer diagnosis as a death sentence.</li> <li>A shortage of primary care physicians and nurses contributes to long wait times for health care in some areas. There are 3 nurses (or midwives) for every 1,000 inhabitants and 2 physicians for every 1,000 inhabitants, this can cause delays in diagnosing women exhibiting breast cancer symptoms early on.</li> <li>Participation rates in the screening program with mammography for women aged 40-74 years are not available. It is inferred that they remain low because close to 45% of breast cancer diagnoses occur at advanced clinical stages (stage III and IV).</li> <li>Mammography units for screening activities are not accredited, which may compromise the quality of the results.</li> <li>A study involving rural and indigenous women found that operational hours of health care services are misaligned with their needs, not considering travel distances. Health care staff identified distance and transportation costs as primary barriers to early detection.</li> </ul>	<ul> <li>Raise awareness of breast cancer symptoms among women.</li> <li>Increase the number of seats in medical and nursing schools.</li> <li>Establish KPIs for the breast cancer screening program, monitor their progress, and make them publicly accessible.</li> <li>Prioritize quality assurance and quality control of mammography units.</li> <li>Health care facilities should tailor their operational hours to accommodate the travel distances and needs of indigenous communities.</li> </ul>					
Diagnostic services						
Challenges	Recommendations					
<ul> <li>An assessment conducted in 2018 found that second-level facilities predominantly used excisional biopsies where the whole tumor or a large part is surgically removed. This method requires a surgeon and can lead to delays in diagnosis.</li> <li>There is a general shortage of radiologists which can lead to delays in the diagnostic process.</li> </ul>	<ul> <li>Continue shifting to needle biopsies.</li> <li>Prioritize recruitment and training of radiologists specialized in breast imaging.</li> <li>Continue ensuring access to biomarker testing for BRCA and PD-L1 status.</li> </ul>					
Treatment						
Challenges	Recommendations					
<ul> <li>There is a shortage of medical oncologists.</li> <li>The number of radiation therapy machines available per capita is insufficient to meet patients' needs based on international recommendations.</li> <li>ION stands as the country's sole oncology hospital and is currently operating at its maximum capacity. Although there were initial plans to construct a new hospital to alleviate this burden, the bidding process for its construction was unfortunately canceled in early 2023 due to insufficient funds.</li> <li>Patients in remote areas face significant challenges in accessing oncology treatment, primarily due to the high costs of transportation, the long distances involved, and the necessity of using various modes of travel.</li> <li>Cancer medicine prices have risen because pharmacies purchase drugs through intermediaries rather than directly from manufacturers, resulting in increased costs and compounded by limited local production.</li> </ul>	<ul> <li>Invest in recruitment and training of medical oncologists.</li> <li>Increase the availability of radiation therapy and explore the use of hypofractionation.</li> <li>Secure funding and optimize the project plan for the new oncology hospital.</li> <li>Develop a comprehensive and integrated health care accessibility strategy for patients living in remote areas.</li> <li>Strengthen the pharmaceutical supply chain and promote domestic</li> </ul>					





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