

Improving outcomes for women with triple-negative breast cancer in Latin America



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IMPROVING OUTCOMES FOR WOMEN WITH TRIPLE-NEGATIVE BREAST CANCER IN LATIN AMERICA

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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. 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.

This present report describes characteristics of TNBC patients and the disease and economic burden to society in five countries in Latin America: Argentina, Brazil, Chile, Colombia, and Mexico. It analyzes key stages – detection, diagnostics, and treatment – along the patient pathway and discusses the societal impact of improved TNBC care. High-level recommendations for improvement of TNBC care are also provided.

The responsibility for the analysis and conclusions in this report lies solely with the authors.

Lund, August 2023

Peter Lindgren
Managing Director, IHE

Executive 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 the United States, the five-year survival rates for TNBC range from 91% in cases diagnosed when the tumor is localized to 12% in cases diagnosed when the tumor has metastasized. 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 used to constitute the only medical treatment option for TNBC patients. Despite the use of chemotherapy, TNBC was characterized by higher tumor recurrence rates and a poorer prognosis compared to all other subtypes. For instance, the five-year survival rate for breast cancer cases diagnosed with regional spread is 66% for TNBC and 83–90% for non-TNBC cases in the United States. 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
- Lack of diagnostic infrastructure
- Lack of comprehensive biomarker testing
- Outdated national clinical guidelines
- 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 have also 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 being able to resume work and surviving TNBC would reduce indirect costs (productivity loss to the economy). Indirect costs of breast cancer are

considerable and almost equally 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 style="list-style-type: none"> ✓ Improve breast cancer prevention ✓ Raise awareness of breast cancer symptoms ✓ Enhance involvement of primary care in early detection ✓ Personalize risk assessment through BRCA genetic testing ✓ Promote participation in screening programs 	<ul style="list-style-type: none"> ✓ Address the underfunding and fragmentation of health care systems ✓ Overhaul national breast screening programs ✓ Establish clear care pathways ✓ Assure high quality of breast cancer imaging ✓ Ensure a swift and complete pathological assessment before treatment start ✓ Recruit and train pathologists, oncologists, and radiologists ✓ Ensure timely availability and utilization of prescribed medicines 	<ul style="list-style-type: none"> ✓ Expand access to comprehensive biomarker testing ✓ Take steps to expand access to appropriate medicines in the public sector ✓ Update local clinical guidelines ✓ Update care pathways and provide training to clinical staff
Key stakeholders		
<ul style="list-style-type: none"> • Patients • Patient advocacy groups • Health care professionals (primary care) • Ministry of Health 	<ul style="list-style-type: none"> • Health care professionals (breast cancer specialists) • Hospitals and diagnostic centers • Ministry of Health 	<ul style="list-style-type: none"> • Medical associations • Hospitals and diagnostic centers • Health care professionals • Ministry of Health

List of abbreviations

ASCO	American Society of Clinical Oncology
BMI	Body mass index
BRCA1/2	Breast cancer gene 1/2
CDK	Cyclin-dependent kinase
ER	Estrogen receptor
ESMO	European Society for Medical Oncology
GDP	Gross domestic product
HER2	Human epidermal growth factor receptor 2
HIC	High-income countries
HRQoL	Health-related quality of life
IARC	International Agency for Research on Cancer
IMSS	Mexican Social Security Institute
KPI	Key performance indicator
NCCN	National Comprehensive Cancer Network
OECD	Organization for Economic Co-operation and Development
PAHO	Pan American Health Organization
PD-L1	Programmed death-ligand 1
PR	Progesterone receptor
TNBC	Triple-negative breast cancer
UHC	Universal health coverage
WHO	World Health Organization

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1. Breast cancer and TNBC

This report focuses on triple-negative breast cancer (TNBC) in Latin America. It describes patient characteristics (chapter 1), the disease and economic burden to society (chapter 2), current challenges in patient access to TNBC care (chapter 3), and the societal impact of improved TNBC care (chapter 4). It also provides a comprehensive set of recommendations for future improvements (chapter 5).

The main geographic focus are five countries in Latin America: Argentina, Brazil, Chile, Colombia, and Mexico. The report builds on a comprehensive review of literature and analysis of official data by public authorities and international organizations.

1.1 Breast cancer

Breast cancer occurs in every country of the world in women at any age after puberty, but with increasing likelihood later in life (1). Breast cancer is the most common type of cancer among women in Latin America and the Caribbean (2). In 2020, an estimated 210,000 new breast cancer cases were diagnosed in the region and 58,000 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. The estimated average lifetime risk for a woman to get breast cancer is close to 9% (2). In countries such as Argentina and Brazil, this risk is even higher (12% and 10%, respectively) and close to rates in high-income countries (HIC) in Europe and Northern America.

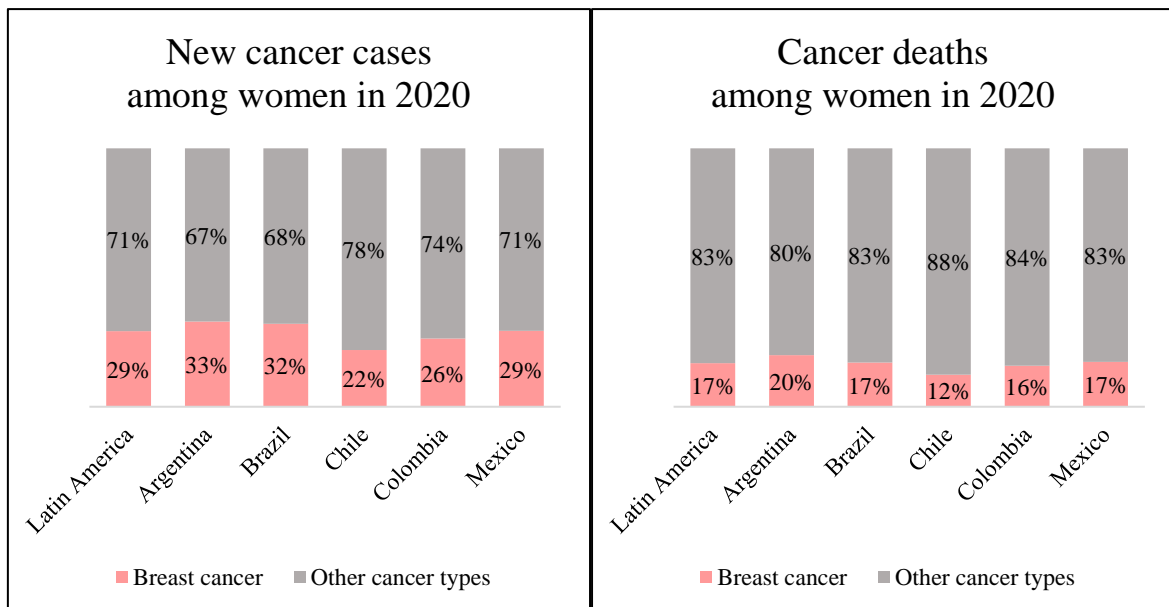


Figure 1: Proportion of new breast cancer cases and deaths among women in Latin America in 2020.

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 (2).

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 (1). 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.

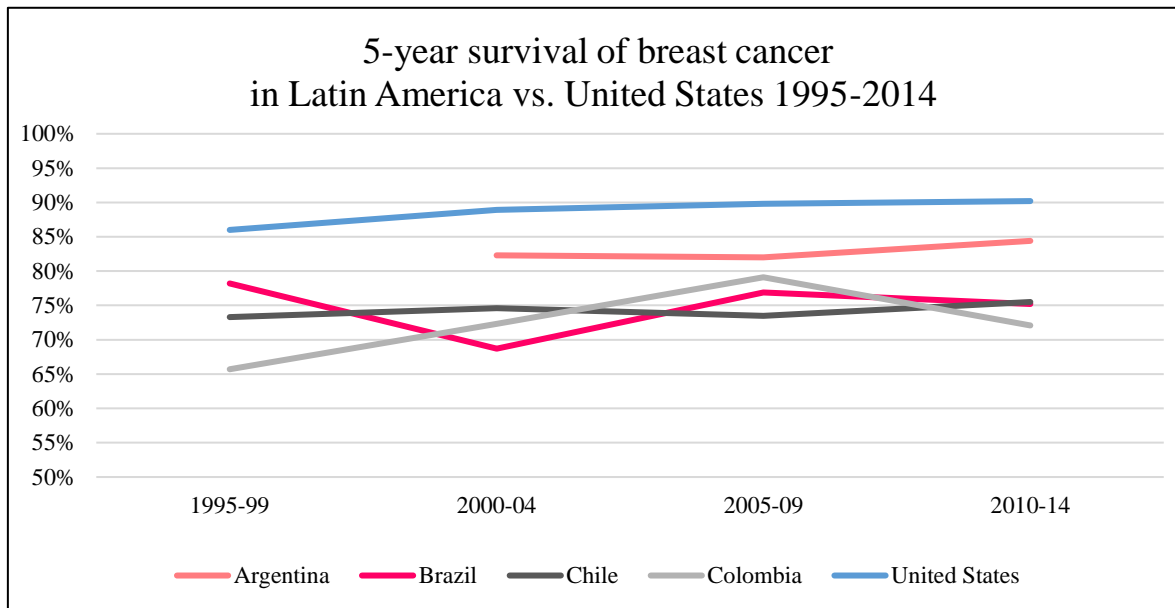


Figure 2: 5-year age-standardized relative survival of breast cancer in Latin American countries and the United States in 1995–2014.

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, and 6.9% and 9.0% in Colombia, respectively. 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) (3). Source: CONCORD (4, 5).

Lower survival rates of breast cancer patients in Latin America than in HIC have previously been attributed to several factors (6):

- 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 to those with private health insurance (7, 8).
- Low rate of early breast cancer detection, leading to 30–40% of cases being diagnosed at an advanced stage compared to only 10% in the European Union. In countries like Colombia or Mexico, around half of detected breast cancer cases are in advanced stages. 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 3.2.

- Poor access to modern treatments, including cancer medicines. 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.

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 (9). *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.

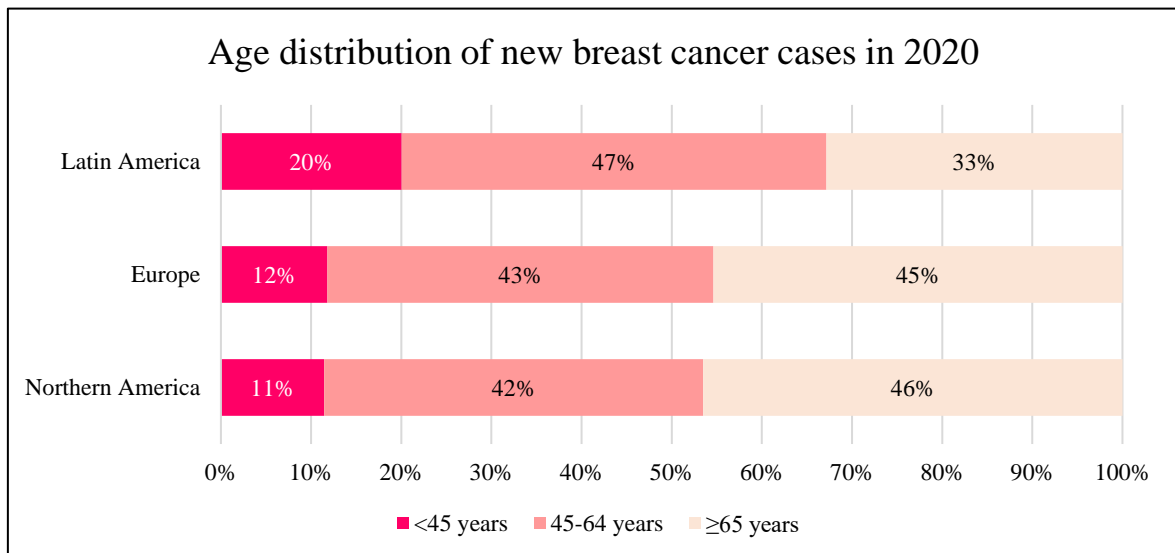


Figure 3: Age distribution of new breast cancer cases in 2020 by world region.

Notes: Latin America includes the Caribbean. Source: Estimates by IARC (2).

1.2 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 (10, 11); 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 (12). The word “negative” in TNBC thus simply refers to the lack of expression of the three receptors.

Table 1: Breast cancer subtypes

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

The treatment of TNBC usually involves 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 (13). Systemic therapy options for TNBC have therefore been restrained to chemotherapy (14), which kills/damages fast-growing tumor cells but also fast-growing healthy cells in the body.

TNBC accounts for around 10–20% of all newly diagnosed breast cancer cases globally (15). Figure 4 shows that the prevalence of TNBC is between 13% and 21% in the selected Latin American countries. These figures are, however, not based on population-based cancer registries, but rather on studies with comparatively small populations. They should therefore be interpreted with caution (16). Nonetheless, several studies have pointed out that TNBC seems to be more frequent in Latin America than in other regions of the world (17).

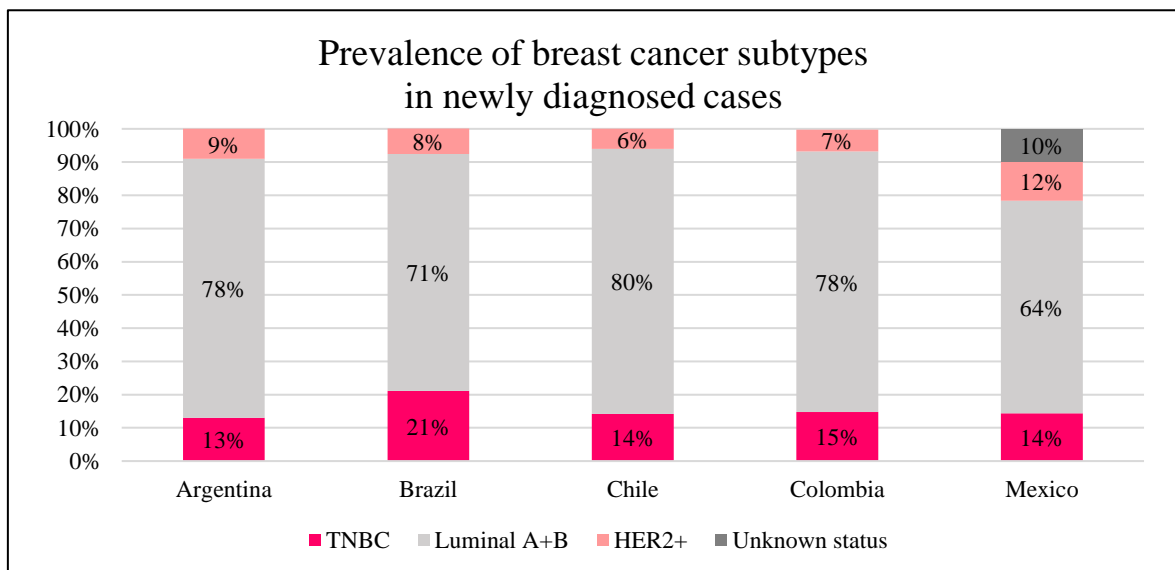


Figure 4: Prevalence of breast cancer subtypes in newly diagnosed cases in Latin America.

Notes: Data for Chile correspond to the average of new breast cancer diagnosis in women ≤ 40 years and ≥ 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. Source: (16, 18-22).

A key feature of TNBC is the younger age at diagnosis compared to other breast cancer subtypes; see Figure 5. The median age at diagnosis is generally below 50 years (23, 24). Young women with breast cancer may face consequences that affect them disproportionately throughout their lives, such

as fertility issues linked to treatment with chemotherapy, a high risk of bone density loss, poor mental health, and lower quality of life (25, 26).

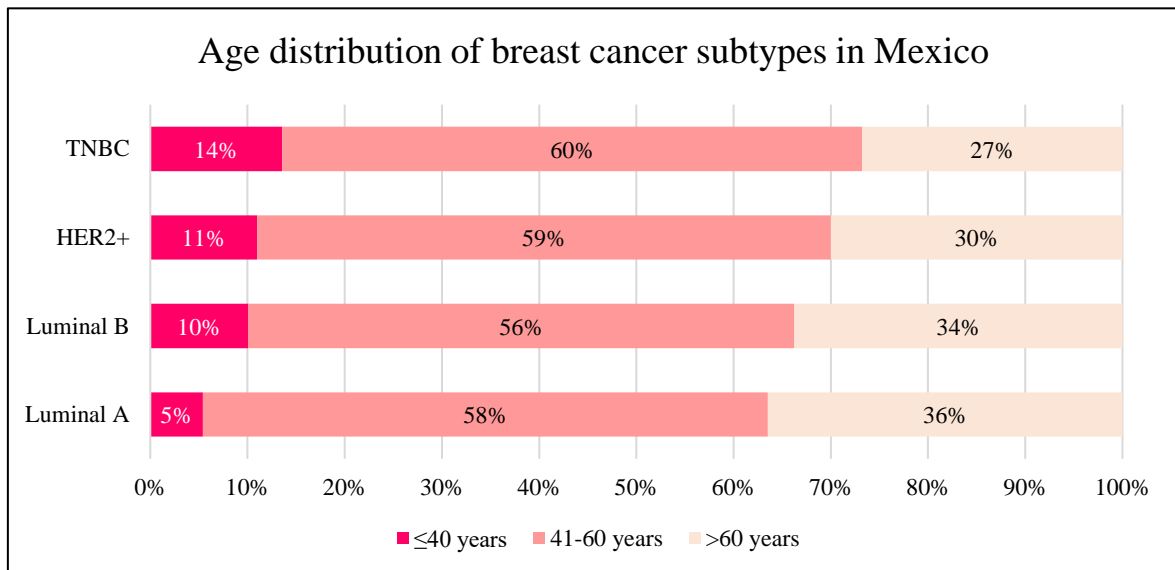


Figure 5: Age distribution of breast cancer subtypes in Mexico.

Notes: Patients diagnosed from January 2011 to December 2014 in two hospitals (n=1502) of the Mexican Social Security Institute (IMSS). Source: (20).

The stage at which TNBC is diagnosed has a significant impact on survival; patients diagnosed later in the disease have a worse prognosis. TNBC tumors tend to grow faster than other breast cancer subtypes (27), 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) (28). In Latin America, TNBC and breast cancer in general is diagnosed late compared with HIC (see also section 3.2). For instance, only 4% and 39% of TNBC cases in Argentina and Colombia might be diagnosed in stage I (see Figure 6), whereas in the United States 61% of TNBC cases are diagnosed at a localized stage (which includes stage I and some cases of stage II).

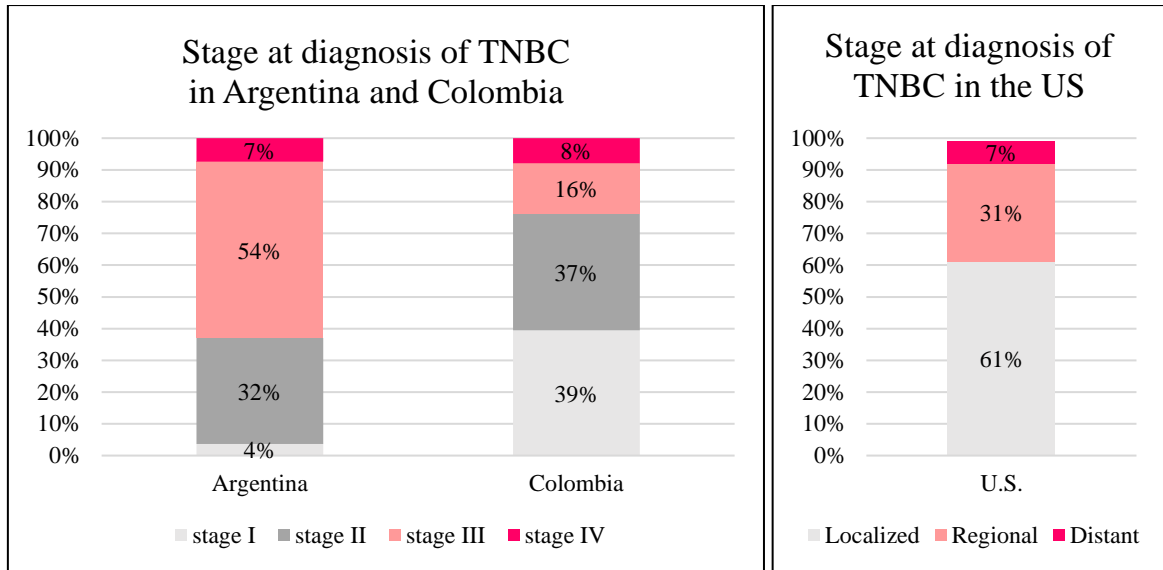


Figure 6: Stage at diagnosis of TNBC in Argentina, Colombia, and the United States.
 Notes: Data for Argentina and Colombia come from very small populations, n=38 and n=28 respectively.
 Source: (18, 29, 30).

1.3 Signs and symptoms of TNBC

Signs and symptoms of TNBC generally resemble those of other breast cancer subtypes. The most common symptoms are shown in Figure 7.

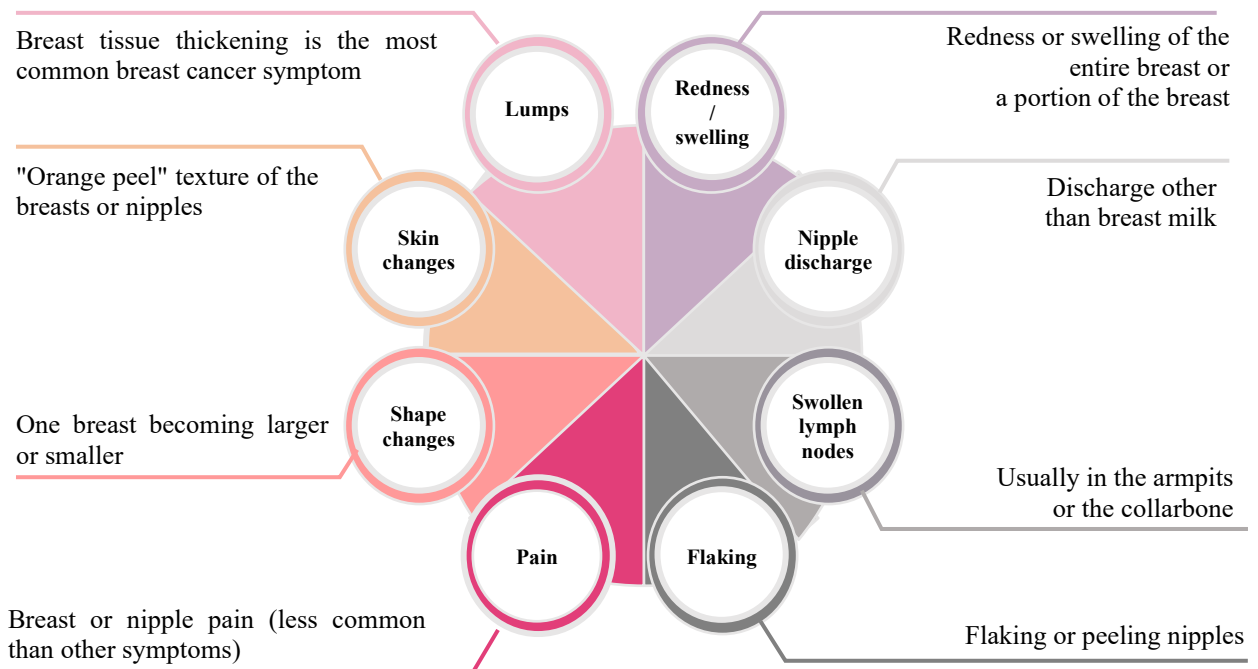


Figure 7: Common signs and symptoms of TNBC.
 Source: (31).

1.4 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) (1).

Table 2: Non-modifiable risk factors in TNBC

Risk factor	General description	Specifics for Latin America
Age	The risk to develop breast cancer increases with age (32). This is also true for TNBC, but TNBC is more common in younger women than other subtypes (see section 1.2).	No studies found on this particular risk factor specific to Latin America
Family history (Heredity)	Approximately 5–10% of all breast cancers have a hereditary background (33). The most common cause of hereditary breast cancer is an inherited mutation in the BRCA1 or BRCA2 gene (33). About 50 out of 100 women with BRCA1/2 mutations will develop breast cancer by the time they turn 70 years, compared to only 7 out of 100 women in the United States (34). Women with BRCA1/2 have a particularly high risk to develop TNBC.	The prevalence of BRCA1/2 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, and 9% in Colombia (35).
Ethnicity	Black and Hispanic women are at an increased risk of developing TNBC compared to Caucasian women but reasons for this are unclear (36, 37). In the United States, black women are nearly three times more likely than Caucasian women to be diagnosed with TNBC (38).	Colombia and Brazil have the largest populations of African descendants (9% and 8%, respectively) from the studied Latin American countries (39, 40). The prevalence of TNBC in Brazil is higher in the north and northeast regions where more women with African ancestry live (21).
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 (41). The link between breast density and developing TNBC is stronger in premenopausal women than in postmenopausal women (38).	No studies found on this particular risk factor specific to Latin America

According to the WHO, at most 30% of all breast cancer cases are theoretically preventable as they are caused by modifiable risk factors (1). A study from Brazil estimated that around 17% of breast cancer cases in postmenopausal women were attributable to modifiable risk factors (42); see Figure 8. The largest modifiable risk factor was obesity and 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 related to obesity/overweight and physical inactivity (43).

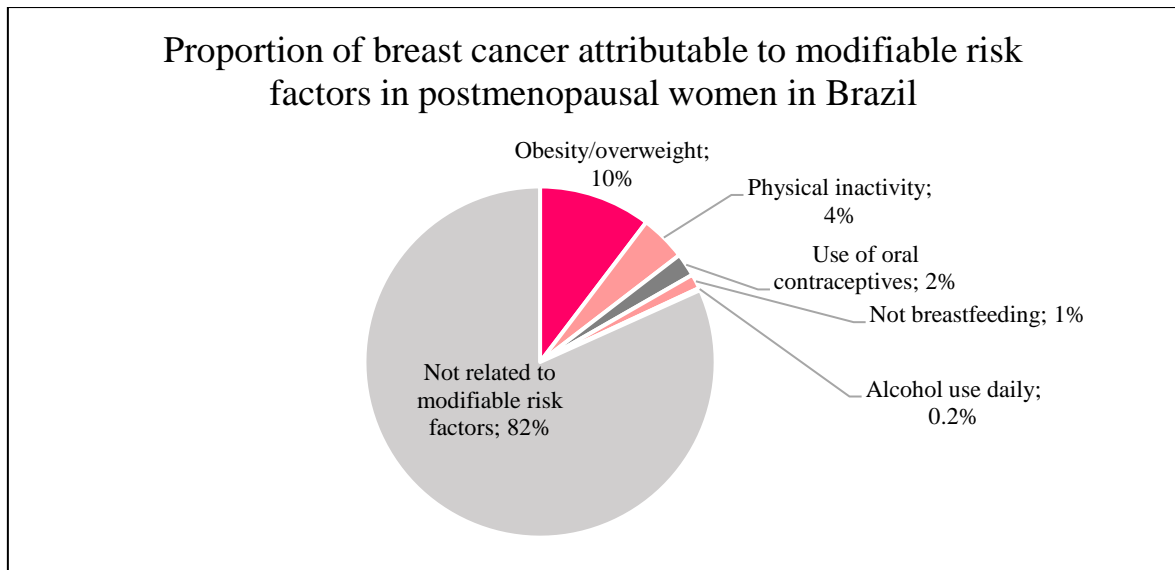


Figure 8: Proportion of breast cancer attributable to modifiable risk factors in postmenopausal women in Brazil.

Source: (42).

Table 3: Modifiable risk factors in TNBC

Risk factor	General description	Specifics for Latin America
Obesity and overweight	Obesity has been linked with a higher likelihood of developing TNBC (44). For breast cancer overall, the link seems to be stronger in postmenopausal women than in premenopausal women (45).	Obesity rates in Latin America are comparatively high. Chile and Mexico are the countries in the OECD with the highest rates of female obesity of over 30% (46). Figure 9 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 (47).	In Latin America, almost half of all women (42%) are physically inactive (46). Countries with the highest prevalence of female physical inactivity are Brazil (53%), Colombia (48%) and Argentina (45%); see Figure 10.
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 (48).	No studies found on this particular risk factor specific to Latin America
No child births	Some studies suggest that having children is associated with a lower risk of hormone-positive breast cancers but with a higher risk of TNBC (49). These studies also indicate that the risk of TNBC increases with the number of births, yet the biological mechanisms for this association are unclear.	No studies found on this particular risk factor specific to Latin America

Notes: Alcohol consumption (50), cigarette smoking (51), hormonal replacement therapy to treat menopausal symptoms (52), and use of oral contraceptives (53) 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 (54, 55).

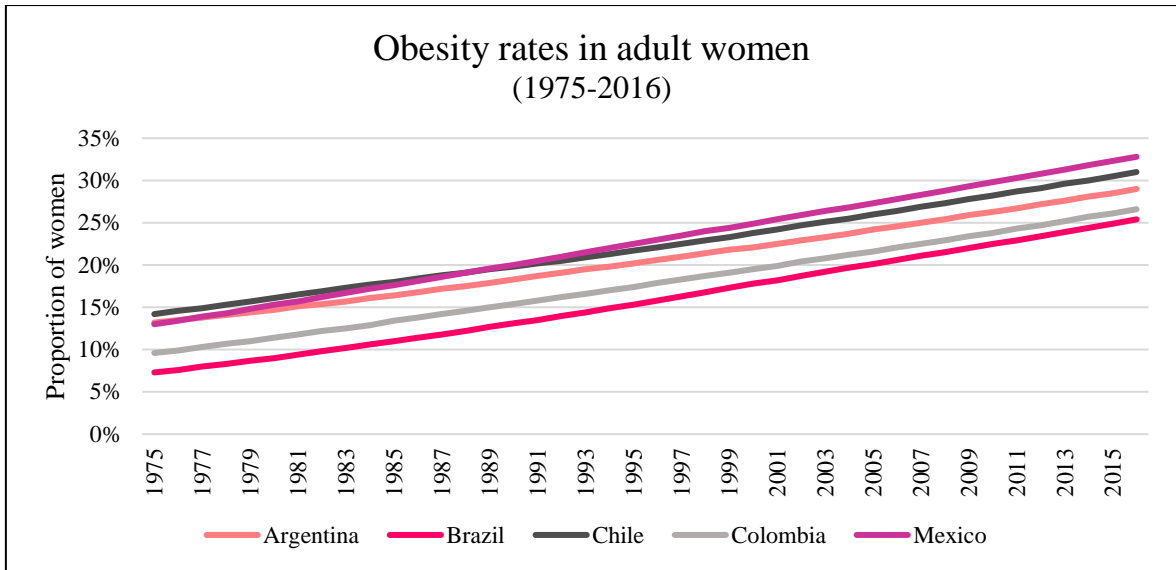


Figure 9: Prevalence of obesity in adult women in Latin America, 1975–2016.

Notes: Obesity is defined as BMI \geq 30. Age group \geq 18 years. Source: WHO (56).

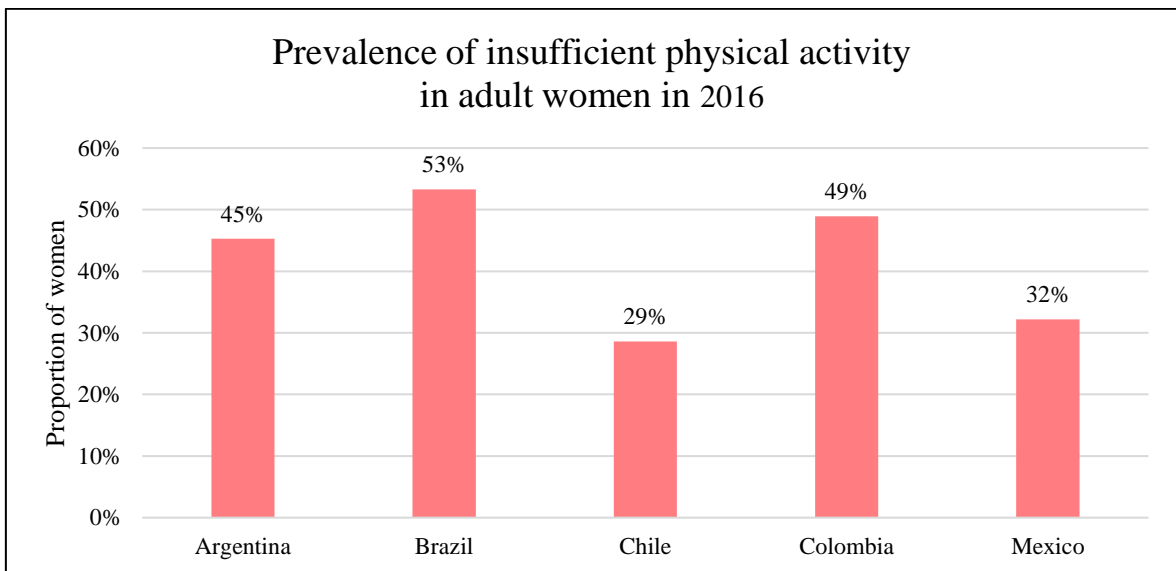


Figure 10: Prevalence of insufficient physical activity in adult women in Latin America, 2016.

Notes: Age group \geq 18 years. Source: OECD (46).

2. Disease and economic burden of TNBC

2.1 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. 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 1.2 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 69 cases per 100,000 women in 2020; see Figure 11. This corresponded to an increase of 112% increase over the whole period. During the same period, the estimated mortality rate of breast cancer increased by 86% from 10 to 18 cases per 100,000 women. The lower relative increase in mortality compared to incidence is a sign of progress in breast cancer care over this period.

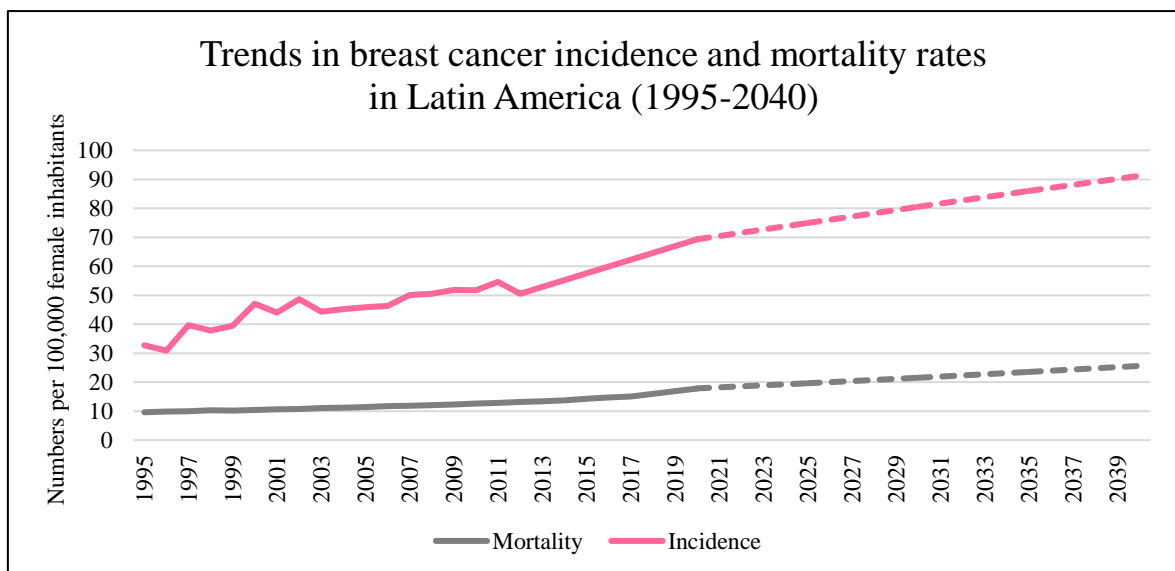


Figure 11: Estimated trends in breast cancer incidence and mortality crude rates per 100,000 female inhabitants in Latin America, 1995–2040.

Notes: The numbers for Latin America are the population-weighted averages of Argentina, Brazil, Chile, Colombia, and Mexico. Numbers between 2020 and 2040 are predictions based on unchanged age-specific risks to get and die from breast cancer. Source: (57-61).

The incidence of breast cancer has not just been increasing in the past in Latin America, but it is also predicted to continue to increase in the future. Figure 11 shows predicted increases until 2040 stemming from demographic changes, in particular population aging.¹ If unfavorable developments in risk factors such as obesity (see section 1.4) continue to increase, this will add to the number of new cancer cases shown in Figure 11.

Figure 12 shows breast cancer incidence and mortality rates in individual Latin American countries in 2020. The country with the highest incidence was Argentina with an estimated 95 cases per 100,000 women. In contrast, Mexico had the lowest incidence rate with 45 cases per 100,000 women. These two countries also had the highest and lowest mortality rates of 30 and 12 deaths per 100,000 women, respectively.

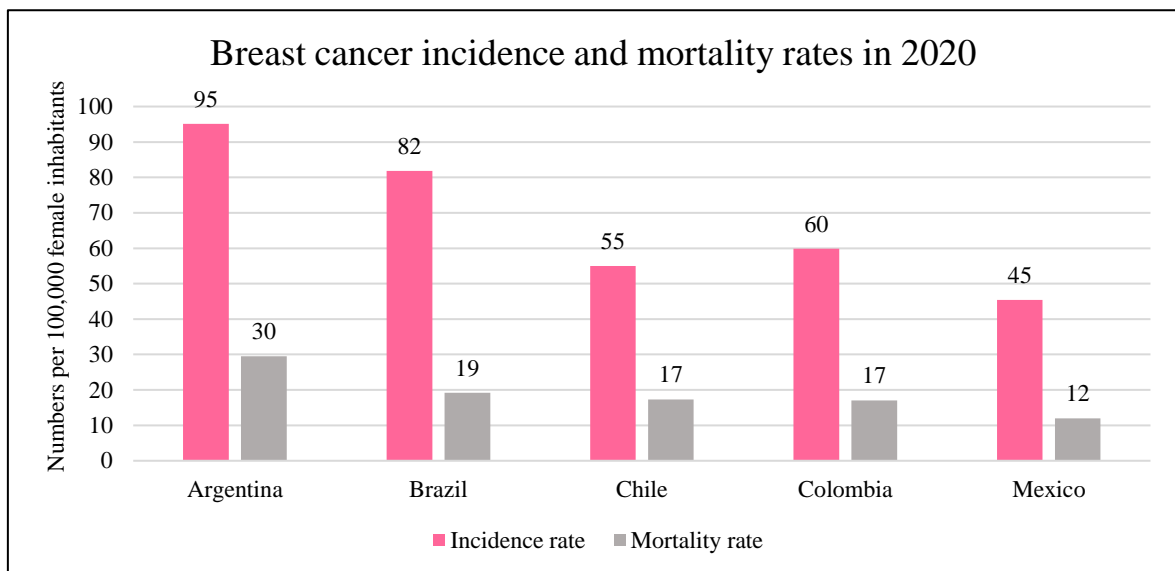


Figure 12: Breast cancer incidence and mortality crude rates per 100,000 female inhabitants in 2020.

Source: Estimates by IARC (2).

2.2 Survival

Survival is a key measure of the disease burden of a cancer type for the individual patient. It measures the likelihood to be 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.

¹ The actual increase in TNBC might be slightly lower because the median age at diagnosis of TNBC is lower than the median age of all breast cancer cases (see section 1.2). The effect of population aging might thus lead to a somewhat less pronounced increase in TNBC compared to other subtypes.

Figure 13 summarizes a collection of 5-year survival data points from different research studies for each country, with 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 was higher than of HER2-positive cancer and similar to that of luminal B breast cancer.

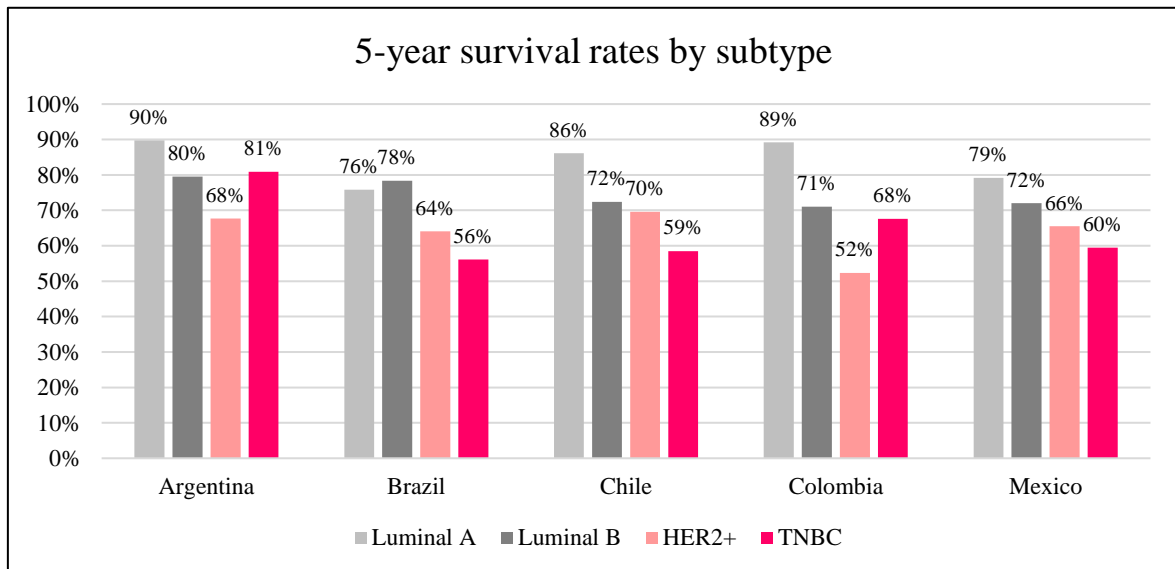


Figure 13: 5-year survival rates by breast cancer subtype in Latin America.

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 (n=366), Colombia absolute survival in 2007–2016 (n=4,059), Mexico absolute survival in 2006–2014 (n=880). Sources: (21, 62-65).

A contributing factor to the comparatively low survival rate of TNBC is its tendency to recur (i.e., come back) after initial treatment (66). While almost 40% of non-metastatic TNBC patients diagnosed in 2004–2012 in Canada experienced recurrence, fewer than 10% of luminal A patients did (67).

The stage at diagnosis of the cancer greatly influences the likelihood of survival. The earlier the diagnosis, the better the prognosis. Figure 14 provides an illustration of this pattern in the United States, given the lack of comparable high-quality data in any Latin American country. When the tumor is still localized at diagnosis, the 5-year relative survival rates of all breast cancer subtypes is close to 100% except for TNBC at 91%. When the tumor has metastasized, the survival rate drops to 12% for TNBC and 32–46% for other subtypes. 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 3.2.

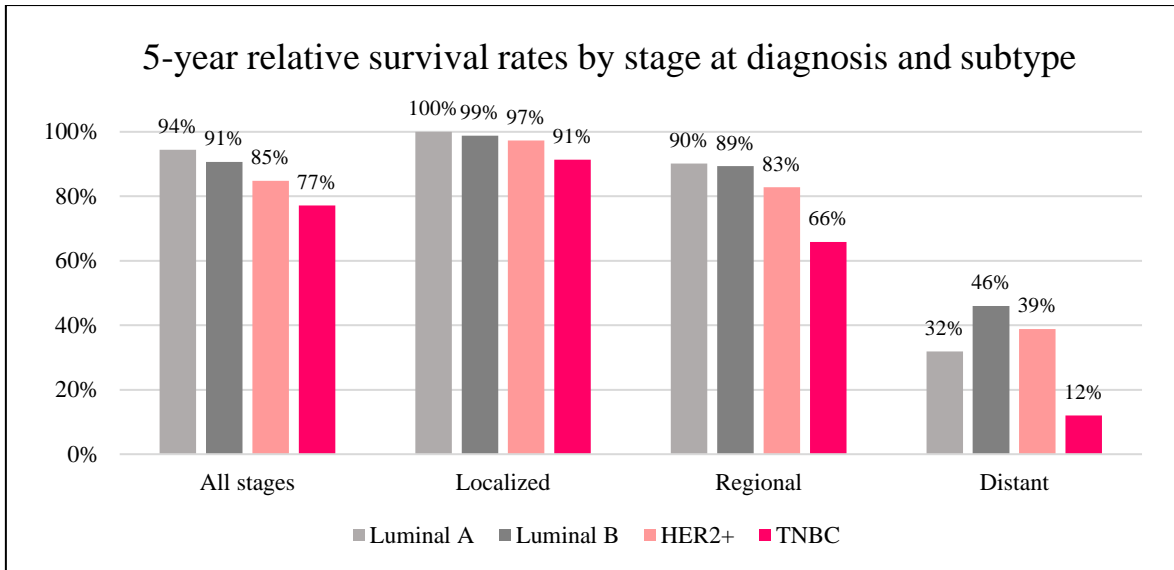


Figure 14: 5-year relative survival rates by stage at diagnosis and breast cancer subtype in the United States (diagnosis period 2012–2018).

Source: SEER (68).

2.3 Economic burden

The burden of TNBC on society can also be measured in monetary terms. The costs of TNBC are here defined more broadly than in an everyday meaning. Generally, three types of costs can be distinguished (69); see Table 4.

Table 4: Components of the economic burden of cancer

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 work due to the disease. They consist of the temporary or permanent inability to work 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.

Comprehensive analyses of the economic burden of breast cancer and TNBC in Latin America are scarce. Figure 15 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 (70). 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.

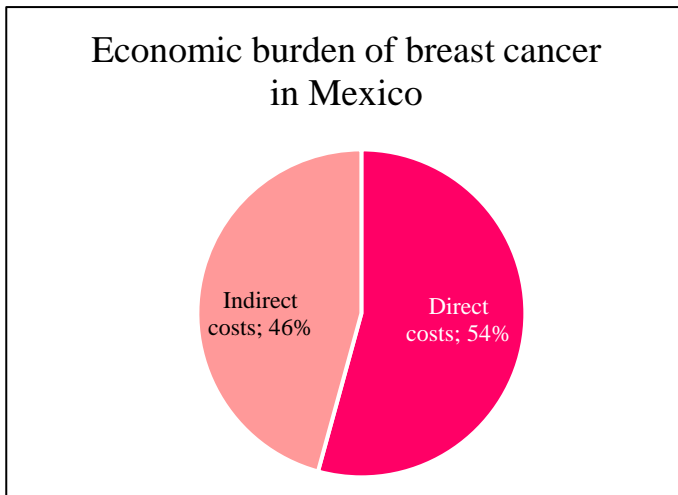


Figure 15: Economic burden of breast cancer patients in public health institutions in Mexico in 2014.

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: (70).

The direct medical costs of breast cancer are composed of the costs of different services received along the patient journey. Figure 16 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 (71).

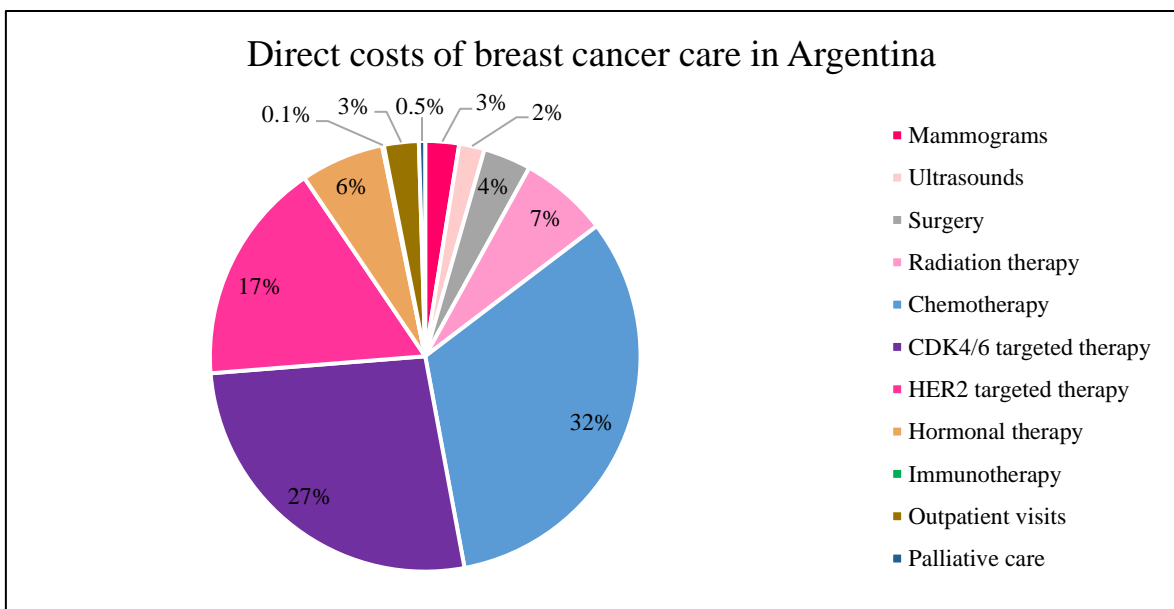


Figure 16: Direct medical costs of breast cancer care in Argentina, 2020. Source: (72).

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 (73-75). 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 high as for stage I (75); see Figure 17. 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 (73).

A similar pattern of late-stage patients being around three to five times more costly to health care systems than early-stage patients has also been found in TNBC in a systematic review of HIC (76); see Figure 17. 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 3.2), would not only save lives but also health care costs.

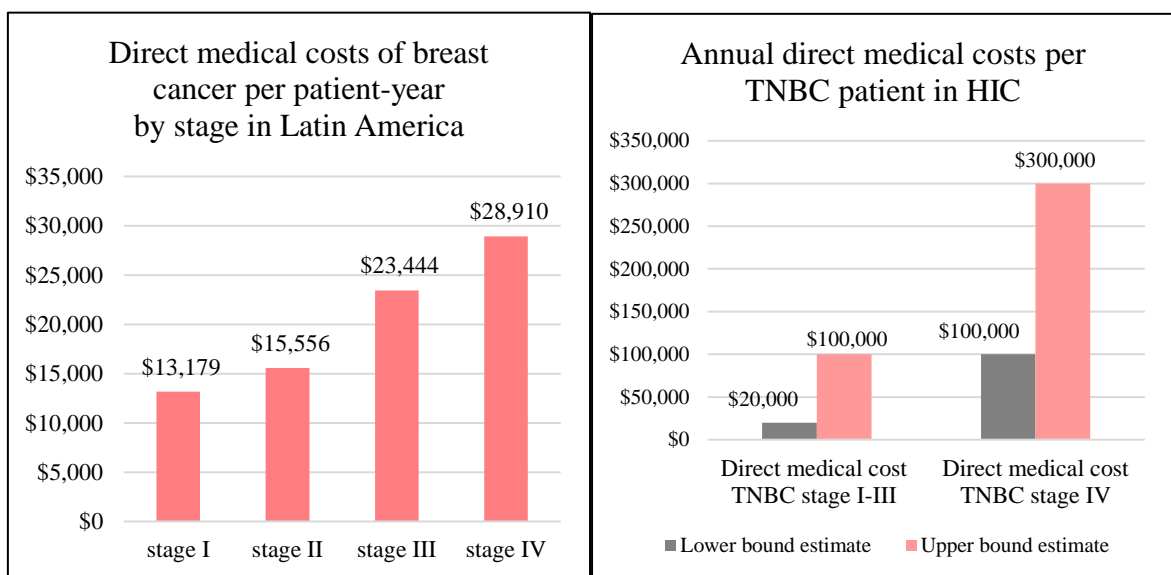


Figure 17: Direct medical costs of breast cancer per patient-year by stage in Latin America (in Int\$) and Range of average annual direct medical costs per TNBC patient by disease stage in HIC (in 2021 USD).

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 US. Source: (75) (76).

3. 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 high-quality care to the entire population are the financing of the health care systems and health insurance coverage (see section 3.1).

TNBC-specific challenges can be found along the entire patient pathway; see Figure 18. The first key stage of the pathway is the detection of breast cancer, which can be triggered through self-detection or through population-based screenings (see section 3.2). 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 3.3.). The third key stage is the treatment (see section 3.4).

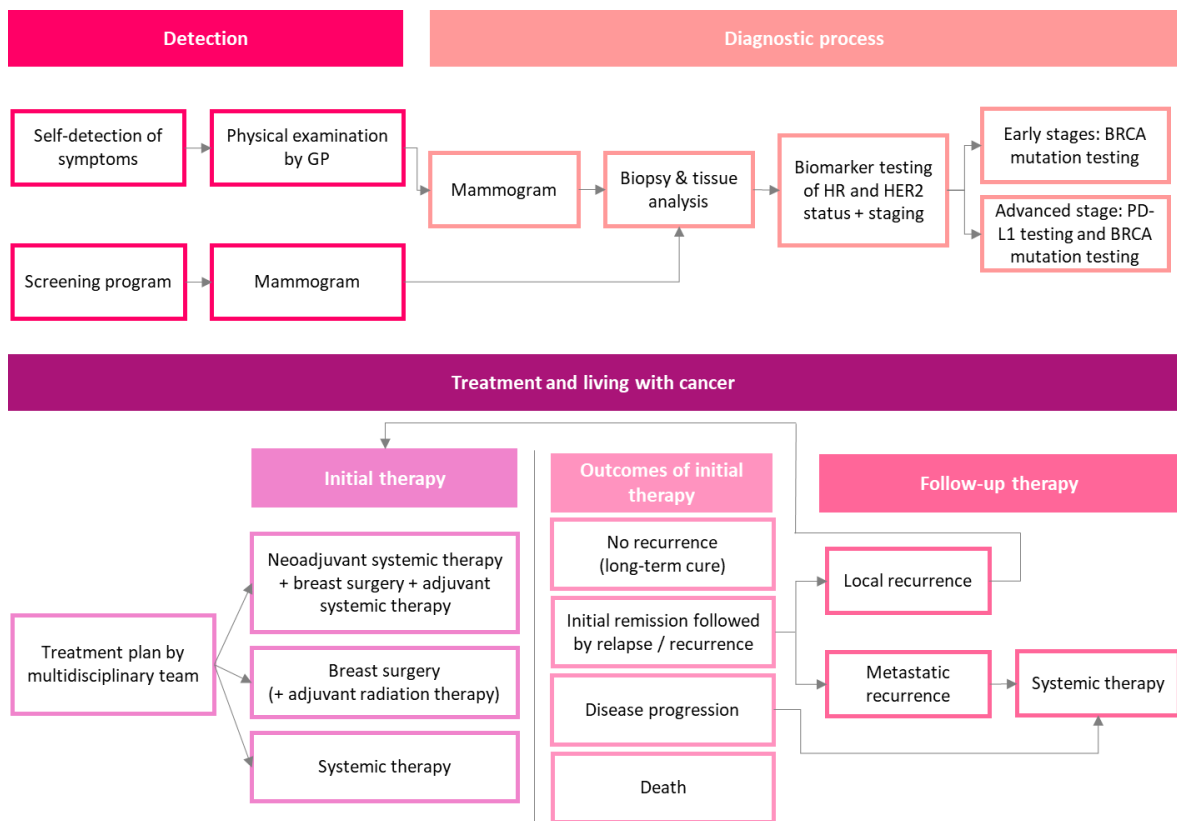


Figure 18: Stylized patient journey in TNBC.

Notes: Based on American Cancer Society and ASCO, ESMO, and NCCN guidelines. Source: (77-80).

In 2021, the WHO established the Global Breast Cancer Initiative to provide strategic guidance and coordination aimed at improving breast cancer care, with a focus on low- and middle-income countries (81). 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 18.

1. Health promotion for early detection (pre-diagnostic interval)

- KPI: >60% of cancer cases are stage I or II at diagnosis.
2. Timely breast 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.

3.1 Health system readiness

The Latin American countries analyzed in this report started reforming their health systems in the 1990s in order to achieve universal health coverage (UHC) (82). Even though UHC in terms of covering the entire population was achieved in 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. According to the WHO index of essential service coverage, coverage ranged from 73 points (out of 100) in Argentina to 80 in Chile in 2019, indicating that a sizable portion of the demand is still unmet (83). In comparison, Spain had an index of 86 points and Canada 89 points (83).

The monetary resources invested in health care differ across Latin American countries. Argentina, Brazil, and Chile spend around 9% of their gross domestic product (GDP) on health care, while Mexico only spends just above 5%. Figure 19 shows how the public portion of total health spending falls short of the Pan American Health Organization's (PAHO) recommended 6% in Brazil, Chile, and Mexico (84). The public expenditure also falls short of the informal WHO's target of 5% public spending in Brazil and Mexico. In absolute numbers, Chile is spending almost \$1400 per capita on health care, compared to around \$900 in Argentina and Brazil and around \$500 in Colombia and Mexico. Mexico is the only country where out-of-pocket expenditure are almost as large as public expenditure, indicating a large financial burden of patients.

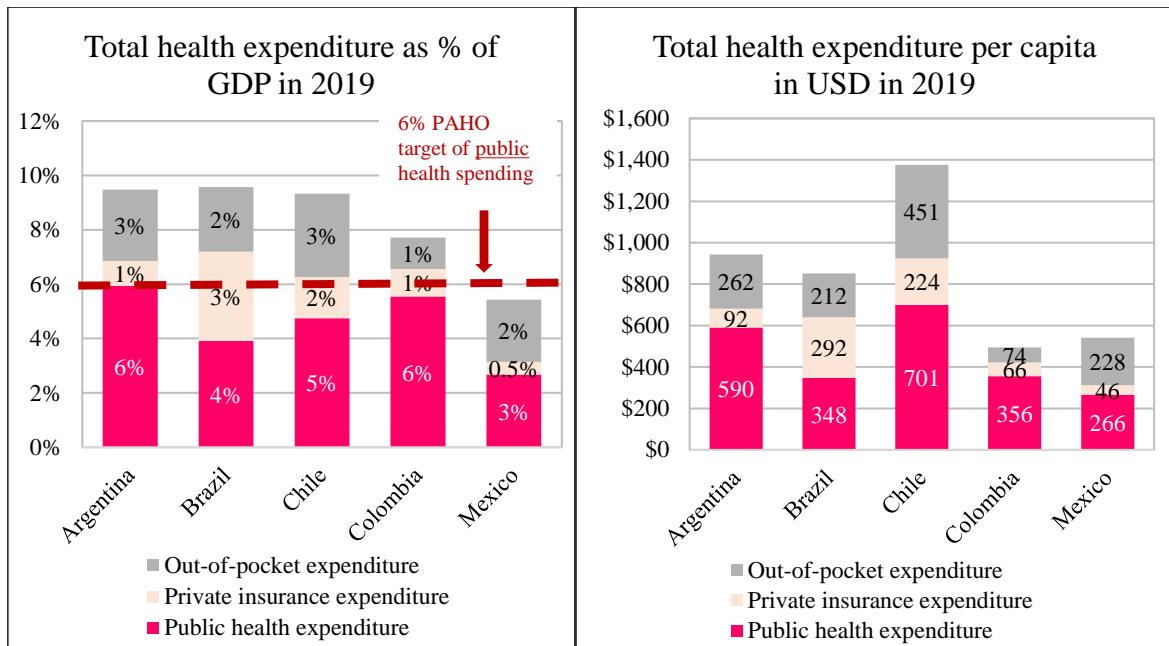


Figure 19: Total health expenditure as percentage of GDP and in USD per capita in 2019.

Notes: GDP = gross domestic product. Expenditure is not adjusted for differences in purchasing power parity. To avoid the impact of COVID-19 on the data for 2020, the figures shown in the graph correspond to the year 2019. However, these 2019 data align with the most recent OECD estimates (at the time of writing this report) for the year 2022 regarding the current health expenditure as a percentage of GDP: 9% for Chile, 8.1% for Colombia, and 5.5% for Mexico. Source: WHO (85).

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 (86). In comparison, around 6% of total health expenditure were spent on cancer care in Europe in 2018 (87).

In addition to being underfunded, the health care systems in Latin American countries are also highly fragmented; see Figure 20 showing the primary provider of health insurance coverage in each country. Argentina's, Colombia's, and Mexico's health care systems are divided into social security regimes for employed and self-employed individuals, private health insurance, and the public health care system for vulnerable populations such as 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 which perpetuates inequalities in access to health care.

For breast cancer care, the fragmentation of the health systems creates two challenges. Firstly, the effectiveness of national breast cancer prevention initiatives is undermined. Secondly, there are profound inequalities in the provision of health services according to insurance coverage.

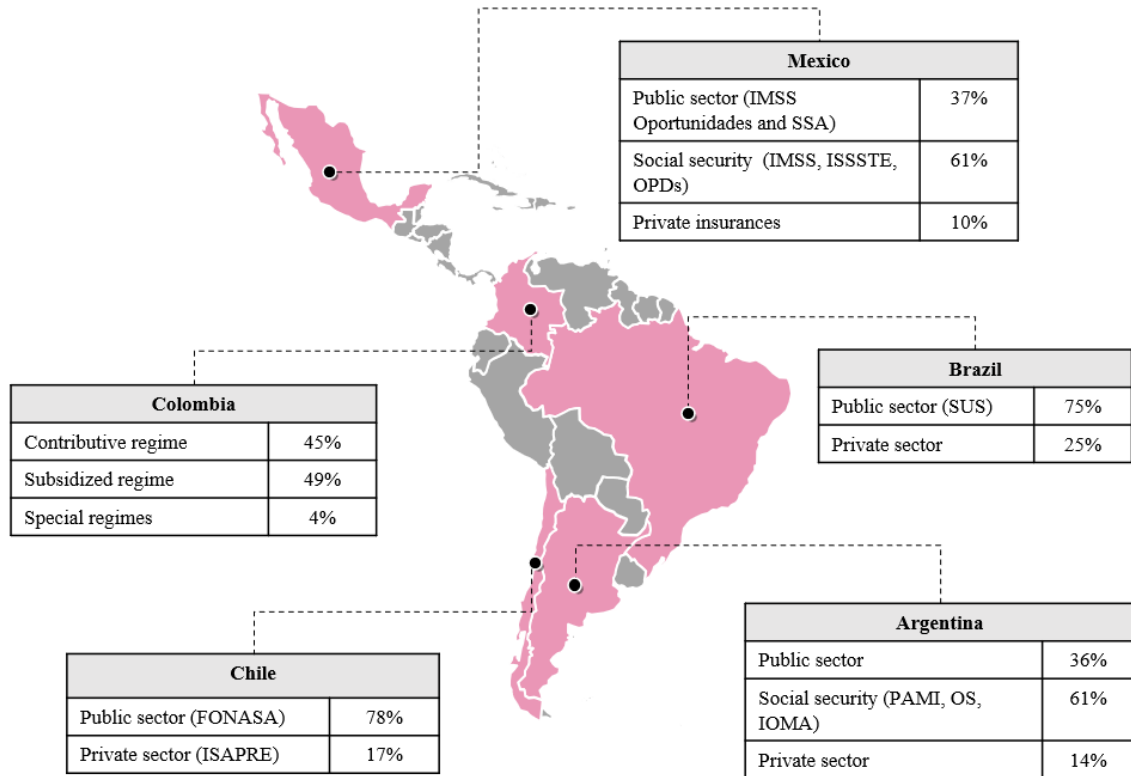


Figure 20: Health insurance coverage (% of population covered) in Latin America.

Notes: The data for Argentina is from the year 2021. As for Brazil, the data for private insurances corresponds to 2021, while the data for public insurances is from 2019. In the case of Chile, the data is from the year 2020, and for Colombia, it is from the year 2022. For Mexico, the data for the public sector and social security is from 2020, and for private insurances, it is from 2021. Source: (88-96).

3.2 Challenges in early detection

Breast cancer may in general be detected in two ways. Firstly, a patient may detect/experience symptoms (see section 1.3) and then consult a health care professional for diagnostic confirmation. Secondly, women who fall into the age group covered by a population-based breast cancer screening program may have an asymptomatic tumor detected on their mammogram.

In Latin America, awareness of symptoms to facilitate self-detection is critical as most countries lack effective screening programs. In Mexico, for example, 84% of breast cancer cases are diagnosed after women have started to develop symptoms, compared to around 50% of cases in HIC (97, 98). The lack of screening programs and/or low participation in these programs in Latin America also contributes to the high percentage of cases diagnosed at advanced stages.

The data shown in Figure 21 compare the difference between the actual rate of early diagnosis of breast cancer at stages I and II and the target of 60% set by the WHO's Global Breast Cancer Initiative. Of all countries analyzed, only Chile surpasses this target.

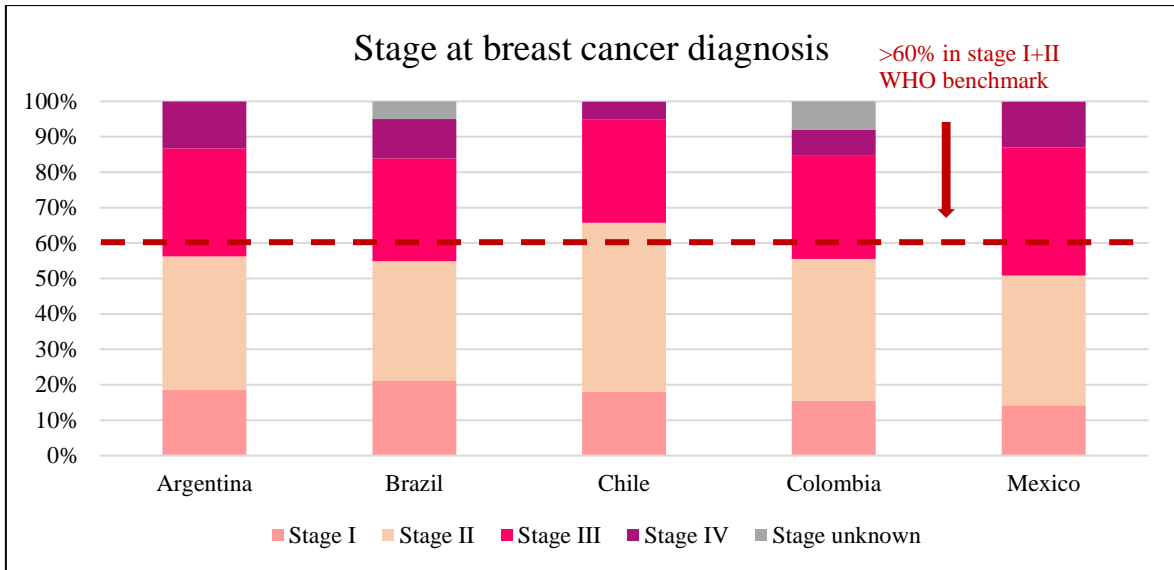


Figure 21: Stage distribution of breast cancer at diagnosis and WHO target.

Notes: Data for Argentina were obtained from the Institutional Registry of Tumors (RITA) and cover cases diagnosed in 2012–2018 (n=9,900), and data were extrapolated excluding the “desc” category. Data for Brazil include cases from the hospital-based cancer registries in 2019. Data for Chile include cases from six public health centers in the Metropolitan Region diagnosed in 2000–2010 (n=5,119). Data for Colombia include all newly diagnosed cases treated in the public sector in 2021 (n=6,593). Data for Mexico include all patients diagnosed at the National Cancer Institute (INCan) with Seguro Popular in 2007–2013 (n=4,300). Sources: (99-104).

Figure 22 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 further below.

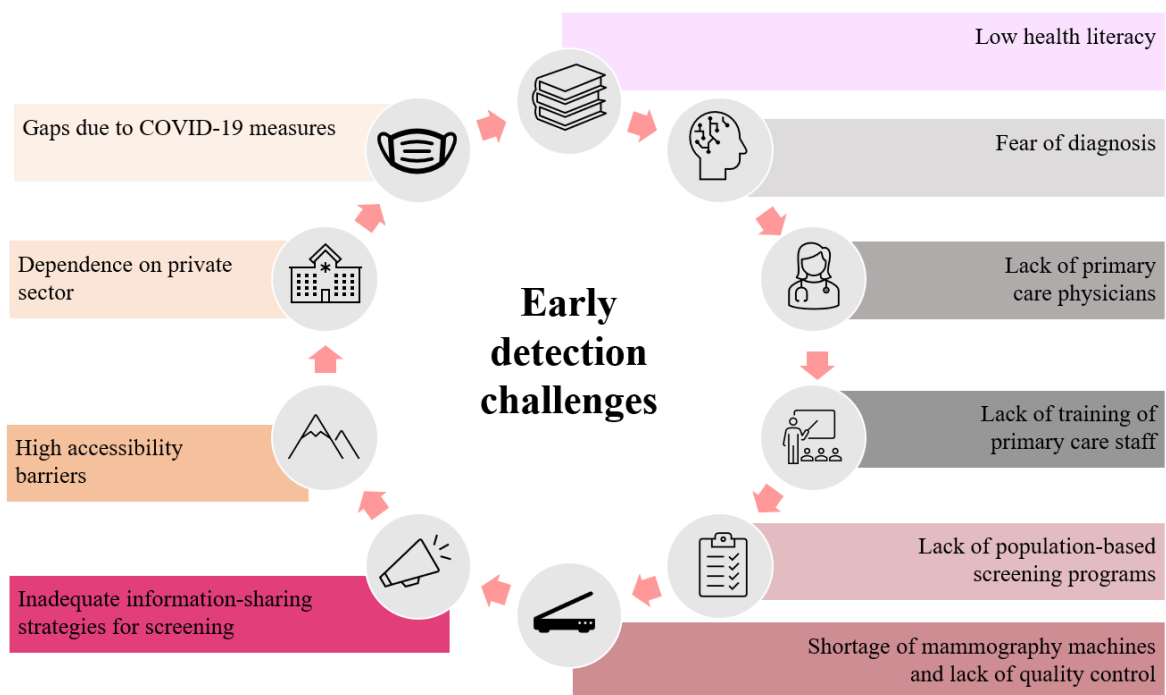


Figure 22: Challenges in early detection of breast cancer in Latin America.

Challenges relating to self-detection

Low health literacy

- According to a poll conducted in 2021, self-detection is preferred by 51% of women in numerous Latin American countries, including Argentina, Chile, Colombia, and Mexico, compared to mammography, which was perceived as the most effective method by only 30% of respondents (105).
- Low awareness of less frequent early signs of breast cancer, such as inverted nipples or changes in the skin were only known by 47% and 41%, respectively, of the women in the survey mentioned above (105).
- 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 (105).
- 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 (106).

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 (107).
- It is estimated that 9% of Mexican women who do not undergo a mammogram are driven by the fear of diagnosis (108).

Lack of primary care physicians

- The OECD has identified the shortage of physicians as a challenge in primary care in Brazil. In 2019, Brazil had one of the lowest rates of practicing physicians among OECD countries, with only 2.3 practicing physicians per 1,000 inhabitants, below the OECD average of 3.5 (109). The ratio of practicing physicians per 1,000 inhabitants in Mexico and Colombia was also below the average, with 2.4 and 2.2, respectively.
- 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 (110).

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 updated with 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 (110).




- 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 to older patients (111). The longer diagnostic intervals were mainly due to physicians at the initial point of contact in the health care system not suspecting breast cancer.



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. The main findings are:

- Participation rates are generally around 30%, with the positive exception of Chile, even in countries where breast cancer screening is subsidized. This is much lower than in HIC; e.g., the average participation rate was 66% in the European Union in 2019 (112).
- The target age group consists usually of women aged 50–69 years, which is narrower than the recommendation by the United States Preventive Services Task Force (50–74 years) and the European Commission (45–74 years) (113, 114). As a larger proportion of women in Latin America gets breast cancer at younger ages than in Europe and the United States, the lower bound 50-year cut-off excludes a sizable group of breast cancer patients.

Table 5: Population-based breast screening programs and results

Country	Early detection strategy	Target population	Results
 Argentina	-The public health care system subsidizes mammography screening and clinical breast exams (115).	-Women aged 50–69, mammography every one or two years. -Screening for high-risk women under 50, with a family history of breast cancer or ovarian cancer.	-32% of the target population gets screened (17). -30% of breast cancer diagnosed at late stages (115).
 Brazil	-Screening is free for the target population (116). -Self-examination is not recommended as a screening method (117) but still many health care professionals teach self-examination techniques (118).	-Women aged 50–69, mammography every two years.	-32% of women aged 50–59 and 25% of the group 60–69 get screened (119). -The availability of mammograms has increased in recent years (120). -40% of breast cancer cases are diagnosed at late stages (121).
 Chile	-Screening is free for the target population (122).	-Women aged 50–69, mammography every three years (122). -Women in high-risk groups outside of this age interval can also receive mammograms.	-More than 70% women aged 50–59 get screened (123). -Significant disparities across socioeconomic groups, with a screening rate of only 34% in low

			socioeconomic groups (124).
 Colombia	-Screening for breast cancer is provided at a population-level.	-Women aged 50–69, mammography every two years. -Annual clinical breast exam starting at age 40.	-Close to 30% of the target population gets screened, with significant disparities across regions (125). -33% of cases are diagnosed in stage III and IV (102).
 Mexico	-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.	- 15 to 25% of the target population gets screened (126) (127). -80 to 90% of cases are diagnosed after stage IIb (126).

Lack of population-based screening programs

- Despite the availability of breast cancer screening programs in all countries except Mexico, some programs appear fragmented, which creates inequalities in access. For instance, Brazil has a population-based screening program, but the efforts are fragmented, which partly explains the low national screening rates in the North compared with the Southeast (119). In Mexico, there are separate efforts as well, 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 (128).

Shortage of mammography machines and lack of quality control

- Scarcity of mammography machines. In Mexico, there are only 9.6 mammography machines per 1,000,000 inhabitants, whereas other countries in the region, such as Colombia, have 14 machines per 1,000,000 inhabitants and the United States has 70.7 machines per 1,000,000 inhabitants (129). 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 lower prices (110).
- 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 mammogram images do not meet the quality standards (130). Approximately 70% of mammography equipment continues to use analogy technology, which has lower image resolution than digital equipment. In Brazil, 40% of all mammography machines are estimated to be working at inadequate levels of quality, increasing the risk of incorrect diagnosis (119). 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 (110). As a result, even if screening rates improve in the future, there is considerable uncertainty about the reliability of test results.

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 (131).
- 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 October. Regarding content, they failed to explain the benefits of early diagnosis or adequately inform Chilean women about the available health care options for them (110).

High accessibility barriers

- 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 expenditure 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% (132). Although more recent data was not found, press releases from 2020 also highlighted lower mammography rates in rural areas in some states of Mexico (133).
- 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% (134). 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 (135).
- 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 (115).
- Accessibility barriers can also be linked to the comprehensiveness of health coverage. In Colombia, patients in the subsidized regime have worse access to care and face greater challenges navigating the patient journey. Only 9% of women in the subsidized regime get diagnosed at stage I, compared to 18% of women in the contributory system (104). In the

subsidized system, 12% of women are diagnosed at stage IV, compared to only 6% in the contributory system (104).

Dependence on private sector

- In Colombia, a study revealed that in 2010, 13% of women paid for mammograms in the private sector (131). 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 to 48% in private facilities (8). Also, 31% of women accessing the public sector were diagnosed at a late stage, compared to 18% in the private sector.
- A study showed that in the private sector in Argentina, 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 (72). Similarly, in Brazil, a study revealed that approximately 40% of cases were diagnosed at advanced stages (III, IV) in the public sector, compared to 16% in the private sector (119).
- 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 (136).

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 to 2019 (137). In Brazil, the number of mammograms performed in the public sector decreased by 42% in 2020 and 15% in 2021 compared to 2019 (138). In Chile, there was a decrease of 62% in breast cancer diagnosis in 2020 compared to 2019 (139). In Mexico, breast cancer screening declined by 79% in 2020 compared to 2019 (140).

3.3 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 (97). Mammography, which is a low-dose X-ray imaging method, is the most common method to diagnose breast cancer. 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 BRCA1/2 mutations in both early-stage and metastatic patients and 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 (79, 80, 141).

Apart from being comprehensive, the diagnostic process should be swift. Keeping the time between diagnosis and treatment start as short as possible increases the chances of survival (142). Breast cancer patients with a long delay of ≥ 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 to patients with a short delay of 0–30 days (143).

Figure 23 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.

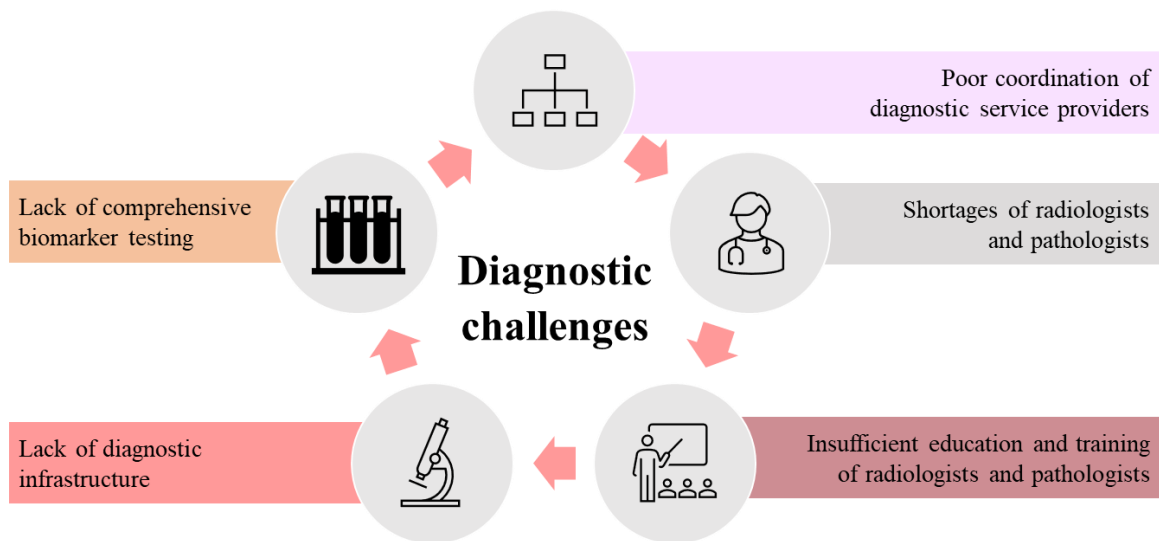


Figure 23: Challenges in the diagnostic process of TNBC in Latin America.

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 (111). This situation and the long waiting times entice women to getting some diagnostic tests 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 quality of service (144).
- In Chile, poor coordination between primary and secondary care levels impede timely referrals and contribute to long wait times (110).

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 in radiologists (130). These shortages lead to long waiting times for essential diagnostic services and thus compels women to rely on services in the private sector with the risk of high out-of-pocket expenditure (145).
- In Brazil, shortages of breast imaging workforce led to long 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 (134).
- 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 (146).
- In Mexico, there are approximately 3 radiologists per 100,000 inhabitants (147), compared to 13 radiologists per 100,000 inhabitants in Europe (148). Even in Brazil, that also faces shortages of breast imaging workforce, the rate of radiologists of 5.8 is higher than in Mexico (147). In all of Mexico, there are only 587 radiologists accredited for breast imaging (149).

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 (110).
- In Argentina, the training of radiology technicians often does not incorporate new technologies (130).

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 gets impaired (150).
- 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 (151).
- In Chile, pathological tests are often not performed in-house but instead sent to different centers, potentially delaying diagnosis (110).
- 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 qualified human resources and insufficient funding makes it difficult to implement this recommendation (152).

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 BRCA1/2 mutations and PD-L1 status are not yet widely implemented.

Table 6: Availability of diagnostic tests for TNBC (November 2022)

Country	Tests for hormone receptor and HER2 status	Tests for BRCA1/2 (with therapeutic intent)	Tests for PD-L1
 Argentina	-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.
 Brazil	- Hormone receptor/HER2 status are routinely done.	-Coverage of comprehensive 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.	- Coverage of comprehensive biomarker testing for PD-L1 status is limited in the public sector by a low coverage cap. -Patient programs pay for testing in both the public and private sector.
 Chile	-Hormone receptor/HER2 status is routinely tested and reimbursed. -The tests may not always happen upfront based on the biopsy, but rather after surgery based on the surgical sample.	-Tests are not reimbursed in the public sector (110). -National clinical guidelines recommend patients with hereditary breast cancer to receive BRCA testing (152).	-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 (104).	-These tests are not reimbursed in the public sector. -Patient support programs by pharmaceutical companies cover the test costs. -National clinical guidelines make no mention of BRCA testing in TNBC (153).	-These tests are not reimbursed in the public sector. -Patient support programs by pharmaceutical companies cover the test costs. -National clinical guidelines make no mention of PD-L1 testing in TNBC (153).

 Mexico	<ul style="list-style-type: none"> -They are considered a good practice (154). -The surgery can be carried out before the test results are available due to some surgeons' reluctance towards neoadjuvant systemic therapy. 	<ul style="list-style-type: none"> -Tests are not reimbursed in the public sector. -Patient support programs by pharmaceutical companies cover the test costs. -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” (154). 	<ul style="list-style-type: none"> -Tests are not reimbursed in the public sector. -Patient support programs by pharmaceutical companies cover the test costs. - National clinical guidelines make no mention of PD-L1 testing (154).
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Notes: Unless sources are provided in the table, information was provided by local experts. Neoadjuvant therapy is the initial therapy and is carried out before surgery.

3.4 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 (including at least a radiologist, radiographer, pathologist, surgeon, medical oncologist, radiation oncologist, breast care nurse, and breast data manager) (97).

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 been historically limited to chemotherapy (155). Since 2018, new options have become available globally with the introduction of immunotherapy and BRCA-targeted therapy in both early-stage and metastatic TNBC. As of 2022, international clinical guidelines by NCCN recommend these novel treatment options (80).

Figure 24 summarizes key challenges associated with the treatment of TNBC in the included Latin American countries. Note that not all challenges apply to every country.

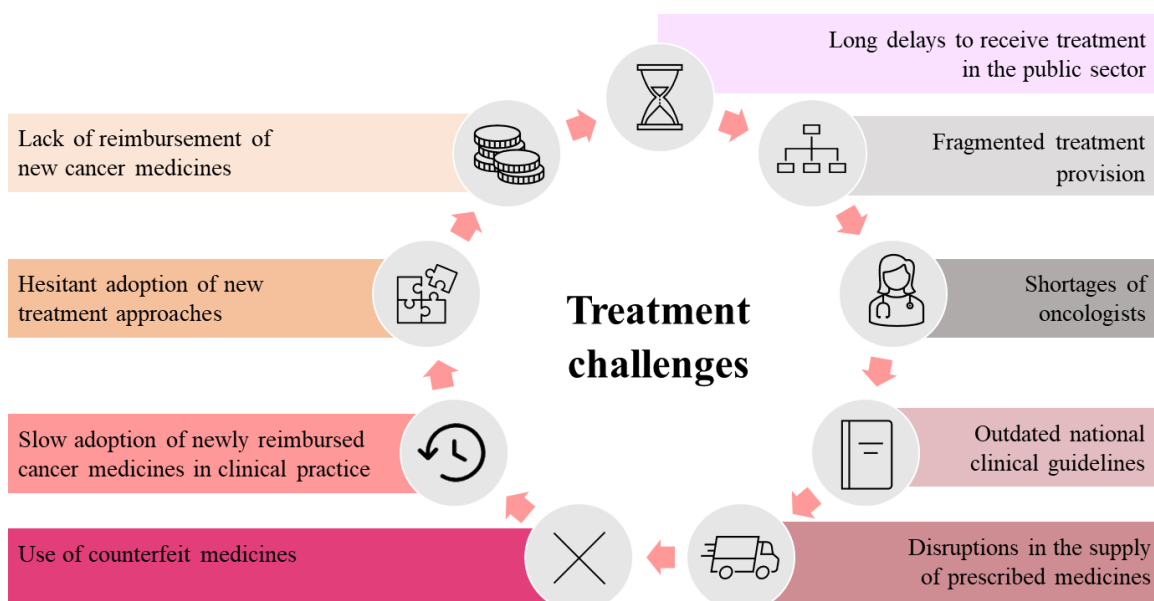


Figure 24: Challenges in the treatment of TNBC in Latin America.

Long delays to receive treatment in the public sector

- In Chile, a law establishes that breast cancer treatment should start within 30 days of being diagnosed (136). In a sample of patients diagnosed in 2017–2018, the mean time from diagnosis to surgery in patients without neoadjuvant treatment (performed before surgery) was 66 days in the public sector and 30 days in the private sector (136).
- 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 (156). 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 to the time before (156).
- In Colombia, the average time between the first medical appointment and receiving chemotherapy is 100 days, and for breast surgery it is 120 days (131). 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 (131).
- In Argentina, according to a study, 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 (157). 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.

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 (158).
- 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 (159).

Shortages of oncologists

- In Colombia, there are only around 250 medical oncologists registered in the national oncology society (131), 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 (160). The lack of medical oncologists can lead to long waiting lists or treatments provided by physicians that are not specialized in cancer treatment (161). In addition, most oncologists are concentrated in the most populated cities, leading to important geographical disparities in access to treatment (131).

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 (153).

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 to only 11% of patients receiving care in private entities (72). Denials of or changes to prescribed medicines are not uncommon (162).

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 (163). In Mexico, COFEPRIS issued a warning in February 2022 that counterfeit lots of immunotherapy were being distributed in the country (164). Counterfeit medicines may put patients at serious risk because they lack active ingredients, contain incorrect doses of active ingredients, contain another active ingredient, etc.

Slow adoption of newly reimbursed medicines in clinical practice

- In Mexico, the process of accessing innovative medicines in hospitals can be sluggish, even when medicines have received regulatory clearance 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 (165). On average, hospitals take 1.6 years to adopt new cancer treatments, whereas new treatments for respiratory diseases and diabetes are adopted in 4 months and 6 months, respectively (165).
- In Colombia, reimbursement of new medicines is associated with the inclusion in the Mandatory Health Plan (POS) (166). However, delays in patient access to new medicines 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.

Hesitant adoption of new treatment approaches

- Treating physicians may be reluctant to adopt new treatment regimens, such as neoadjuvant (performed before surgery) or adjuvant treatments (performed after surgery) in TNBC in patients that 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 therapies (performed before surgery) in the studied countries, underutilization of these therapies in breast cancer has been reported in Europe and the US (97, 167). As well as a reluctance to prescribe neoadjuvant treatments to women with high-risk early-stage breast cancer by Australian surgeons (168).

Lack of reimbursement of new cancer medicines

- Patient access to newer cancer medicines is generally low in Latin America (169). The percentage of cancer medicines approved worldwide in 2014–2020 with full reimbursement by public payers in the selected countries in 2022 ranged from 0 to 21%, while 64–70% of medicines were not reimbursed in any way; see Figure 25. 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 (86). In comparison, spending on cancer medicines accounted for 31% of total cancer care expenditure in Europe in 2018 (69).

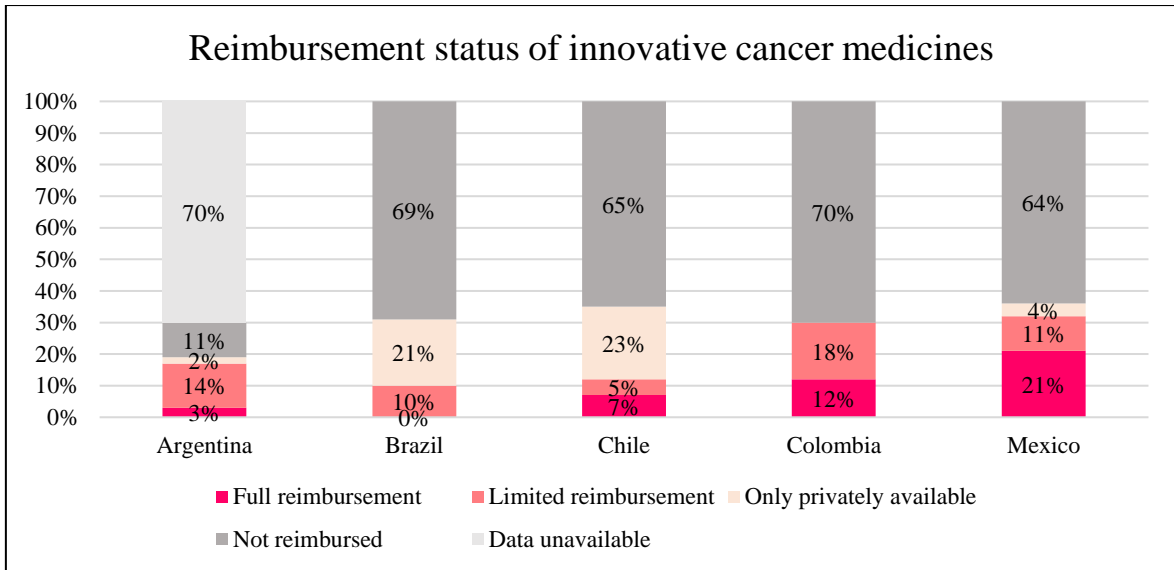


Figure 25: Reimbursement status of cancer medicines approved worldwide in 2014–2020 on June 1st, 2022.

Notes: The sample contains 100 cancer medicines. The Argentinian dataset was incomplete. Source: FIFARMA Patients WAIT Indicator 2022 survey (169).

4. 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 also has wider implications for society. Figure 26 depicts different elements of the societal impact of TNBC. Apart from health outcomes, this includes effects on work life and family life as well as the need for informal care and economic implications.

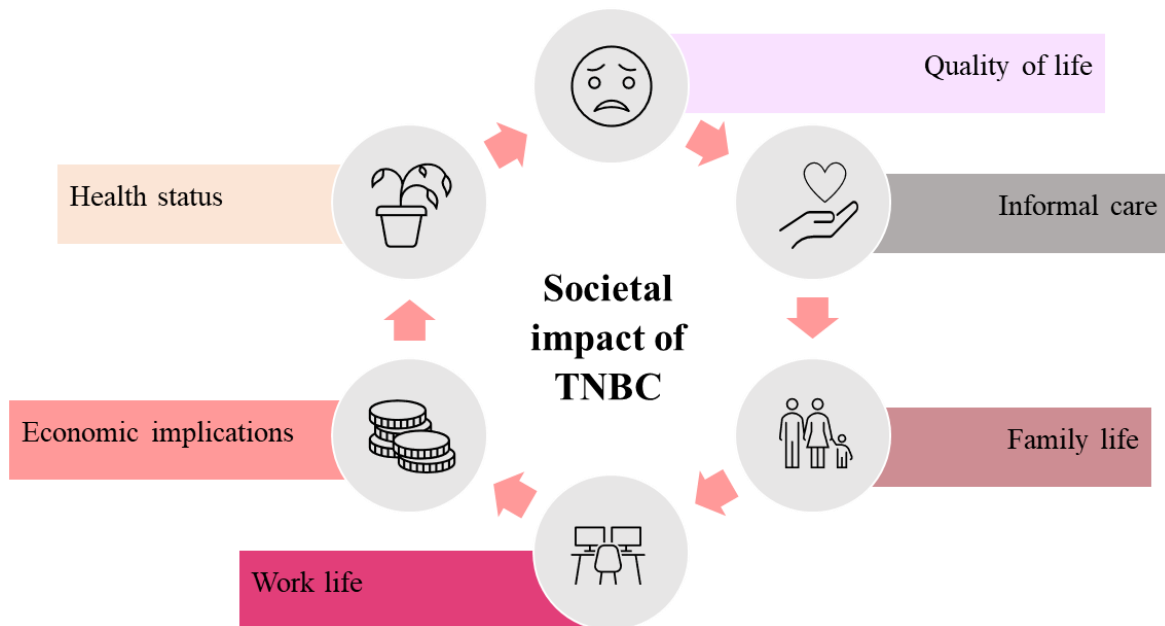


Figure 26: Elements of the societal impact of TNBC.

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., five-year survival rate of 91% in stage I but only 12% in stage IV in the United States (68); see section 2.2).
- **Family life and informal care:** The lower symptom burden of breast cancer in early 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 at early stages than at late stages. Indeed, the per-patient-year medical costs for stage IV breast cancer are more than twice as high as for stage I breast cancer in Latin America (75); see section 2.3. The increased number of women surviving TNBC and being able to resume work would also reduce the indirect costs (productivity loss).

5. 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 might 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 27. The implementation of these recommendations will require the cooperation of various stakeholders in each area. This includes foremost patient advocacy groups, health care professionals (both in primary care and breast cancer specialists), hospitals and diagnostic centers, medical associations, and the Ministry of Health.

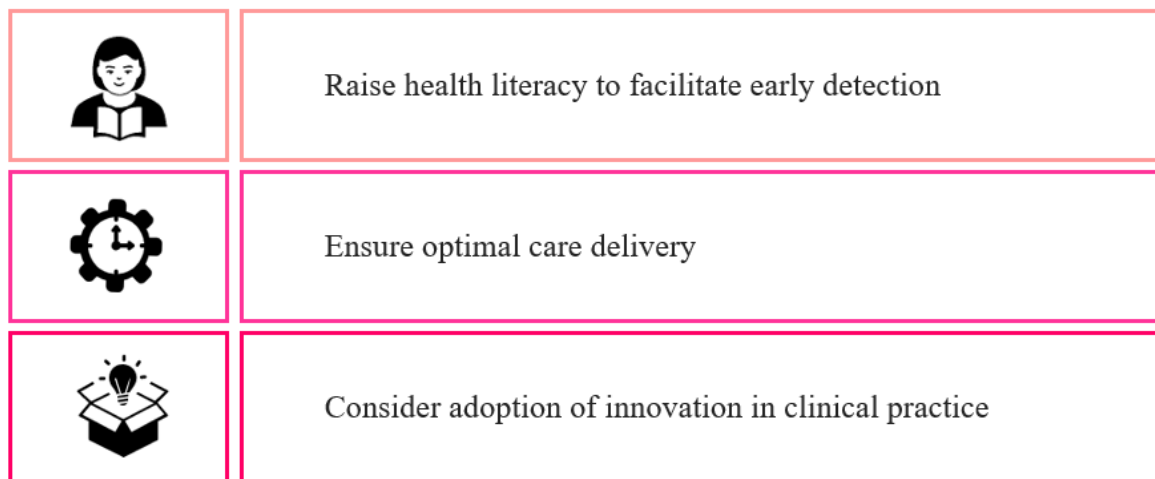


Figure 27: Main areas of improvement for TNBC care.

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, in particular by 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 health literacy and regular self-examination 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

Uncovering genetic risks can help to pay particular attention to early symptoms of breast cancer. Many women with BRCA1/2 mutations are unaware of having 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.

Promote participation in screening programs

Apart from Chile, all Latin American countries have comparatively low participation rates in breast cancer screening programs. Raising women's knowledge of the potential benefits and harms of participating in organized 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

Despite the existence of national screening programs in many Latin American countries (with the notable exception of Mexico), only around 30% of women in the target population get screened. Many reasons for these low screening rates have been identified. This includes (i) lack of awareness of the benefits of screening, (ii) low number of mammography machines, (iii) uneven geographical distribution of mammography machines, (iv) lack of clarity about which screening facility to attend, (v) long waiting lists to get a screening appointment, (vi) 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 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.

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 (medical oncologists), 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) until 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 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.

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.

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 BRCA1/2 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 therapeutic approach. Adequate testing infrastructure also needs to be put in place. Currently, these tests are not fully covered in the public sector across Latin American countries. Tests are typically accessible only through special patient access programs or are paid for by patients out-of-pocket.

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. Clinical staff needs to be trained to ensure optimal use of novel treatment options.

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Annex – Country cards



Argentina

Population: 46.2 million ⁽²⁰²²⁾
 GDP per capita: USD 13,686 ⁽²⁰²²⁾
 Life expectancy: 75 years ⁽²⁰²¹⁾
 Total health expenditure: 9.9% of GDP ⁽²⁰²⁰⁾
 Source: World Bank

Triple-Negative Breast Cancer (TNBC)

- Breast cancer is the most common cancer type in women (33% of all new cancer cases) and responsible for 20% of all female cancer deaths.
- Around 13% of new breast cancer cases are of the TNBC subtype.
- 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 style="list-style-type: none"> • Inadequate health care access despite universal health coverage. According to the WHO, the average coverage of essential health care services is only 73 points out of 100, lower than in Mexico, Brazil, Colombia, and Chile (74, 75, 78, and 80, respectively). This indicates that a significant portion of the demand for essential health care remains unmet. • Inequities in access to care in the public vs. the private sector. Publicly insured patients face longer delays in accessing virtually all health care services. For instance, in the private sector, 42% of breast cancer cases are diagnosed early in clinical stage I, compared to only 17% in the public sector. • The fragmented health care system impedes national efforts for breast cancer prevention and control programs. • Almost 30% of the female population is obese and 45% of women are not sufficiently physically active, which increases the risk to get breast cancer. 	<ul style="list-style-type: none"> • Continue the development of the health system to achieve better coverage of all essential health care services to the entire population. • Strive for a more equitable distribution in the provision of health care services between the public and the private sector. • Create effective national prevention strategies to halt rising levels in obesity and physical inactivity.

Early detection

Challenges	Recommendations
<ul style="list-style-type: none"> • 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 many times underestimate the severity of symptoms leading to delays in going to a medical checkup. • The national breast cancer screening program for women aged 50–69 only achieves a participation rate of 32%, despite the public sector subsidy for mammograms. Low participation partly explains why around 30% of breast cancer diagnoses are made at an advanced clinical stage. • Many mammograms do not meet quality standards, and most of the mammography machines use analog technology with lower accuracy than digital technology. • Due to COVID-19 control measures, disruptions in the cancer screening program and changes in patient behavior have led to reductions in screening. 	<ul style="list-style-type: none"> • Raise awareness of breast cancer symptoms among women. • Run public campaigns to increase participation in the breast screening program. • Implement fixed appointments and reminders for the breast cancer screening program. • Prioritize quality assurance and quality control of mammography machines. • Intensify efforts to boost participation in breast cancer screening in the aftermath of the COVID-19 pandemic.

Diagnostic services

Challenges	Recommendations
<ul style="list-style-type: none"> • Bottlenecks in the public health system limit the number of available appointments for diagnostic services for people with breast cancer symptoms. In the public sector, breast cancer patients wait on average 50 days to get a diagnosis compared to 18 days in the private sector. • Shortages in radiologists and inadequate radiology technician training with courses that do not incorporate new technologies contribute to the lack of available essential diagnostic services. • Testing for HER2 is routinely performed but usually takes longer than testing for hormone receptor status, because the payment for the HER2 test is dependent on the patient's health insurance, and the clinician must request the test before pathologists can perform it. • Comprehensive biomarker testing for BRCA 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. 	<ul style="list-style-type: none"> • Establish clear and rapid care pathways for breast cancer patients in the public sector. • Invest in recruitment and skills of health care professionals in radiology. • Ensure upfront HER2 testing by default. • Expand access to biomarker testing for BRCA and PD-L1 status.

Access to treatment

Challenges	Recommendations
<ul style="list-style-type: none"> • There are problems with the public supply of medicines. Even if the compulsory medical plan covers them, breast cancer patients may experience denials of medicines or changes in prescribed medicines. • Limited access to appropriate cancer care in the public sector. The FIFARMA Patients WAIT Indicator 2022 survey indicated that patients in the public sector only have full access to 3% of all cancer medicines launched globally in 2014–2020. 	<ul style="list-style-type: none"> • Address supply shortages of prescribed medicines. • Enhance patient access to cancer medicines in the public sector.



Brazil

Population: 215.3 million ⁽²⁰²²⁾
 GDP per capita: USD 8,918 ⁽²⁰²²⁾
 Life expectancy: 73 years ⁽²⁰²¹⁾
 Total health expenditure: 10.3% of GDP ⁽²⁰²⁰⁾
 Source: World Bank

Triple-Negative Breast Cancer (TNBC)

- Breast cancer is the most common cancer type in women (32% of all new cancer cases) and responsible for 17% of all female cancer deaths.
- Around 21% of new breast cancer cases are of the TNBC subtype.
- 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 style="list-style-type: none"> • 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. • 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. • The fragmented health care system with a high reliance on the private sector impedes national efforts for breast cancer prevention and control programs. • 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. 	<ul style="list-style-type: none"> • Continue the development of the health system to achieve better coverage of all essential health care services to the entire population. • Strive for a more equitable distribution in the provision of health care services between the public and the private sector. • Create effective national prevention strategies to halt rising levels in obesity and physical inactivity.

Early detection

Challenges	Recommendations
<ul style="list-style-type: none"> • 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. • 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. • The organization of the screening program is inadequate. Eligible women for screening are not systematically identified and invited. • Insufficient mammography equipment coverage, primarily in the North and Northeast. • Many mammography machines operate at inadequate levels of quality, increasing the risk of incorrect diagnosis. • Due to COVID-19 control measures, disruptions in the cancer screening program and changes in patient behavior have led to reductions in screening. 	<ul style="list-style-type: none"> • Strengthen the role of primary care in early detection of breast cancer. • Run public campaigns to increase participation in the breast screening program. • Implement fixed appointments and reminders for the breast cancer screening program. • Improve geographical access to mammography screening. • Prioritize quality assurance and quality control of mammography machines. • Intensify efforts to boost participation in breast cancer screening in the aftermath of the COVID-19 pandemic.

Diagnostic services

Challenges	Recommendations
<ul style="list-style-type: none"> • There is a shortage of specialists involved in the imaging of breast cancer, which leads to delays in the diagnostic process. • 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. • Coverage of comprehensive biomarker testing for BRCA 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 	<ul style="list-style-type: none"> • Invest in recruitment and skills of health care professionals in breast imaging. • Consolidate diagnostic services and ensure safe transportation of samples to external laboratories. • Expand access to biomarker testing for BRCA and PD-L1 status.

Access to treatment

Challenges	Recommendations
<ul style="list-style-type: none"> • The FIFARMA Patients WAIT Indicator 2022 survey indicated that patients do not have full access in the public sector to any new cancer medicines launched globally in 2014–2020. Only 10% of these medicines have a CONITEC recommendation, but without centralized purchasing 	<ul style="list-style-type: none"> • Enhance patient access to cancer medicines in the public sector.



Chile

Population: 19.6 million ⁽²⁰²²⁾
 GDP per capita: USD 15,356 ⁽²⁰²²⁾
 Life expectancy: 79 years ⁽²⁰²¹⁾
 Total health expenditure: 9.1% of GDP ⁽²⁰²¹⁾
 Source: World Bank

Triple-Negative Breast Cancer (TNBC)

- Breast cancer is the most common cancer type in women (22% of all new cancer cases) and responsible for 12% of all female cancer deaths.
- Around 14% of new breast cancer cases are of the TNBC subtype.
- 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 style="list-style-type: none"> • Inequities in access to care in the public vs. the private sector. 78% of the population is covered by the public insurance and 17% by private insurances. 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. • 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. • 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. 	<ul style="list-style-type: none"> • Strive for a more equitable coverage of health care services across the public and private health care regimes (FONASA and ISAPRES). • Increase public funding of cancer care. • Create effective national prevention strategies to halt rising levels in obesity and physical inactivity.

Early detection

Challenges	Recommendations
<ul style="list-style-type: none"> • 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. • 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. • The national breast cancer screening program aimed at women aged 50 to 69 achieves a 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. • Even though a medical order is not required today, women rely on the advice of primary care health professionals to get a mammogram. • 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. • 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. • Due to COVID-19 control measures, disruptions in the cancer screening program and changes in patient behavior have led to reductions in screening. • In primary care, there is a high turnover of health professionals. 	<ul style="list-style-type: none"> • Strengthen the role of primary care in early detection of breast cancer. • Raise awareness of breast cancer symptoms among women. • Improve information-sharing strategies about screening to low socioeconomic groups. • Prioritize quality assurance and quality control of mammography machines in the public and private sector. • Intensify efforts to boost participation in breast cancer screening in the aftermath of the COVID-19 pandemic. • Develop continuing medical education plans for health professionals in primary care.

Diagnostic services

Challenges	Recommendations
<ul style="list-style-type: none"> • 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. • 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. • 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). • Comprehensive biomarker testing for BRCA 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. 	<ul style="list-style-type: none"> • Establish clear and rapid care pathways for breast cancer patients in the public sector. • Prioritize investment in pathology services and training of pathologists. • Ensure that all women are tested upfront for hormone receptor/HER2 status. • Expand access to biomarker testing for BRCA and PD-L1 status.

Access to treatment

Challenges	Recommendations
<ul style="list-style-type: none"> • Limited access to appropriate cancer care in the public sector. The FIFARMA Patients WAIT Indicator 2022 survey indicated that patients in the public sector only have full access to 7% of all cancer medicines launched globally in 2014–2020. 	<ul style="list-style-type: none"> • Enhance patient access to cancer medicines in the public sector. • Address the disparity in TNBC, as it represents the only group of breast cancer patients without access to new treatments.



Colombia

Population: 51.9 million ⁽²⁰²²⁾
 GDP per capita: USD 6,630 ⁽²⁰²²⁾
 Life expectancy: 73 years ⁽²⁰²¹⁾
 Total health expenditure: 8.9% of GDP ⁽²⁰²⁰⁾
 Source: World Bank

Triple-Negative Breast Cancer (TNBC)

- Breast cancer is the most common cancer type in women (26% of all new cancer cases) and responsible for 16% of all female cancer deaths.
- Around 15% of new breast cancer cases are of the TNBC subtype.
- 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 style="list-style-type: none"> 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. 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. The fragmented health care system impedes national efforts for breast cancer prevention and control programs. 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. 	<ul style="list-style-type: none"> Strengthen the provision of essential health care services in the public sector overall. Strive for a more equitable coverage of health care services, with a focus on the subsidized regime. Create effective national prevention strategies to halt rising levels in obesity and physical inactivity.

Early detection

Challenges	Recommendations
<ul style="list-style-type: none"> 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. 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. 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 habit. Women must wait a long time to schedule appointments for breast cancer screenings. Unclear public information about which medical facility women should visit to get screened. Despite the screening program being for free, many women still opt to pay for mammograms in the private sector due to quality concerns. 	<ul style="list-style-type: none"> Raise awareness of breast cancer symptoms among women. Run public campaigns to increase participation in the breast screening program. Implement fixed appointments and reminders for the breast cancer screening program, including information about which clinic to visit. Increase the availability of mammography machines to reduce waiting times. Prioritize quality assurance and quality control of mammography machines.

Diagnostic services

Challenges	Recommendations
<ul style="list-style-type: none"> 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. 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. Comprehensive biomarker testing for BRCA 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. 	<ul style="list-style-type: none"> Invest in recruitment and training of pathologists. Ensure upfront testing for hormone receptor/ HER2 status for all patients by default. Expand access to biomarker testing for BRCA and PD-L1 status.

Access to treatment

Challenges	Recommendations
<ul style="list-style-type: none"> 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. There is a shortage of medical oncologists. 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. 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. There is a lack of patient access to new cancer medicines. The FIFARMA Patients WAIT Indicator 2022 survey indicated that patients in the public sector only have full access to 12% of all cancer medicines launched globally in 2014–2020. Outdated national clinical guidelines for breast cancer treatment from 2017. 	<ul style="list-style-type: none"> Improve the coordination between different cancer care service providers. Invest in recruitment and training of medical oncologists. Improve the bureaucracy to ensure patients can receive prescribed medicines. Enhance patient access to cancer medicines in the public sector. Update national clinical guidelines for TNBC.



Mexico

Population: 127.5 million ⁽²⁰²²⁾
 GDP per capita: USD 11,091 ⁽²⁰²²⁾
 Life expectancy: 70 years ⁽²⁰²¹⁾
 Total health expenditure: 6.2% of GDP ⁽²⁰²⁰⁾
 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 responsible for 17% of all female cancer deaths.
- Around 14% of new breast cancer cases are of the TNBC subtype.
- 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 style="list-style-type: none"> 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 asymptotically 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. 	<ul style="list-style-type: none"> 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 inactivity.

Early detection

Challenges	Recommendations
<ul style="list-style-type: none"> 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. 	<ul style="list-style-type: none"> 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

Challenges	Recommendations
<ul style="list-style-type: none"> 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 BRCA 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. 	<ul style="list-style-type: none"> 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 BRCA and PD-L1 status.

Access to treatment

Challenges	Recommendations
<ul style="list-style-type: none"> 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 2022 survey indicated that patients in the public sector only have full access to 21% of all cancer medicines launched globally in 2014–2020. Use of counterfeit medicines puts patients at serious risk. 	<ul style="list-style-type: none"> Enhance patient access to cancer medicines in the public sector. Strengthen legislation to combat the use of counterfeit medicines.

The Swedish Institute for Health Economics (IHE) is an independent research institute grounded in health economics. Together with clients from the public, private and civic sectors, we strive to provide evidence for sound decision making. We work in Sweden, rest of Scandinavia and internationally, studying a wide range of issues related to health and health care.

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