Improving outcomes for women with triple-negative breast cancer in Asia-Pacific

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Foreword

Breast cancer is the most common cancer type in women in Asia-Pacific. Of the different subtypes of breast cancer, triple-negative breast cancer (TNBC) is the most challenging 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 markets in the Asia-Pacific region: Australia, Hong Kong, South Korea, Taiwan, and Thailand. 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, April 2023

Peter Lindgren
Managing Director, IHE

Executive summary

In the Asia-Pacific region, breast cancer is a major and growing public health concern, accounting for 23% of all new cancer cases and 14% 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 9–13% 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 Taiwan, the five-year survival rate in TNBC ranges from 95% in cases diagnosed in stage I down to 11% in cases diagnosed in stage IV. Affecting slightly younger women than other breast cancer subtypes, TNBC tumors also tend to grow faster than other subtypes. This makes early detection – through self-detection and screening – particularly crucial. Current challenges for early detection of TNBC in Asia-Pacific include:

- Unawareness of early signs of breast cancer and cultural beliefs about cancer resulting in a reluctance to consult health care services upon noticing symptoms
- Inadequate knowledge of primary care staff of breast cancer symptoms
- Absence of organized population-based screening programs, such as in Hong Kong and Thailand
- Non-participation in screening programs due to various misconceptions such as the misbelief that “breast cancer is not going to happen to me”
- Low participation in screening programs of women with low socioeconomic status and women living in rural areas

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 hormone receptors and HER2 receptors that are targeted by hormonal therapy and HER2-targeted therapies, respectively. For this reason, 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 than all other subtypes. For instance, the five-year survival rate for breast cancer cases diagnosed in stage III in Taiwan is 59% for TNBC and 77% for non-TNBC cases. 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 Asia-Pacific include:

- Geographical barriers to access diagnostic imaging services
- Shortages of radiologists required for diagnostic imaging
- Lack of reimbursement and quality control of diagnostic imaging exams
- Uncoordinated organization of diagnostic testing
- Lack of comprehensive biomarker testing
- Delays to receive treatment in the public sector partly caused by a lack of health care staff
- Delay or refusal of treatment by patients due to factors such as fear of surgery, poor quality of life following treatment, fear of treatment-related adverse effects
- Use of alternative non-prescribed treatments by patients
- High patient copayments for cancer care services
- 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 medical costs of TNBC diagnosed in stage IV (NZ$ 65,000) were 2.5 times higher than in stage I (NZ$ 26,000) according to a study from New Zealand. This is similar to the situation in high-income countries in Europe and North America, where per-patient medical costs ranged from around US$ 20,000–100,000 in stage I–III TNBC to around US$ 100,000–300,000 in stage IV TNBC.
- ✓ 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 equally large as treatment costs according to a study from South Korea, 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 the Asia-Pacific region. 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**
✓ 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 ✓ Tailor screening promotion campaigns to women in vulnerable groups	✓ Invest in recruitment and retention of primary care workers ✓ Implement breast cancer screening programs and guarantee free access ✓ Broaden the target age group in screening programs ✓ Establish clear care pathways ✓ Assure high quality of breast cancer imaging ✓ Recruit and train radiologists for breast imaging ✓ Support patient adherence to treatment	✓ Expand access to comprehensive biomarker testing ✓ Update local clinical guidelines ✓ Update care pathways and provide training to clinical staff
Key stakeholders		
• Patients • Patient advocacy groups • Health care professionals (primary care) • Ministry of Health	• Health care professionals (breast cancer specialists) • Hospitals and diagnostic centers • Ministry of Health	• Medical associations • Hospitals and diagnostic centers • Health care professionals • Ministry of Health

List of abbreviations

ASCO	American Society of Clinical Oncology
BCNA	Breast Cancer Network Australia
BMI	Body mass index
BRCA1/2	Breast cancer gene 1/2
CEWG	Cancer Expert Working Group on Cancer Prevention and Screening
CSMBS	Civil servant medical benefit scheme
ER	Estrogen receptor
ESMO	European Society for Medical Oncology
ESMO-MCBS	ESMO Magnitude of Clinical Benefit Scale
GDP	Gross Domestic Product
HER2	Human Epidermal Growth Factor Receptor 2
HRQoL	Health-related quality of life
IARC	International Agency for Research on Cancer
KPI	Key performance indicator
MRI	Magnetic resonance imaging
MBS	Medicare Benefits Schedule
NCCN	National Comprehensive Cancer Network
NGO	Non-governmental organization
NHI	National Health Insurance
OECD	Organisation for Economic Co-operation and Development
OOP	Out-of-pocket
PD-L1	Programmed death-ligand 1
PR	Progesterone receptor
SSS	Social security scheme
TNBC	Triple-negative breast cancer
UCS	Universal coverage scheme
UHC	Universal health coverage
US FDA	Food and Drug Administration in the United States
WHO	World Health Organization

Table of contents

1. Breast cancer and TNBC

This report focuses on triple-negative breast cancer (TNBC) in Asia-Pacific. 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 and locations, referred to as "*markets*" in the remainder of the report, in the region: Australia, Hong Kong, South Korea, Taiwan, and Thailand.

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 cancer among women in Asia and Oceania (2). In 2020, an estimated 1.05 million new breast cancer cases were diagnosed in the region and around 351,000 women died from the disease. In Asia and Oceania, breast cancer is responsible for 23% of all new cancer cases and 14% of all cancer deaths in women; see Figure 1. The estimated average lifetime risk for a woman to get breast cancer is close to 6% (2). In places like Australia the risk is much higher at 15%, which is comparable to the situation in Europe and Northern America.

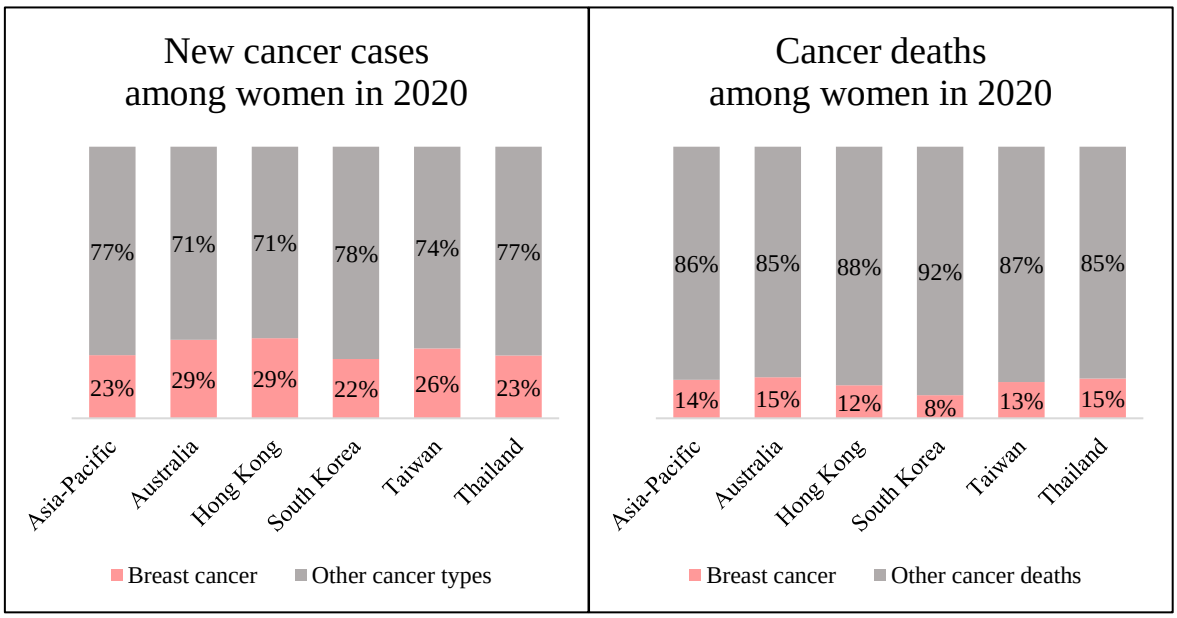

Figure 1: Proportion of new breast cancer cases and deaths among women in Asia-Pacific in 2020.
Note: Cancer was defined as all types excluding non-melanoma skin cancer. Asia-Pacific includes all countries across Asia and Oceania. Mortality data for South Korea are from 2019. Source: IARC and national cancer registries (2-7).

In high-income countries across the globe, 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 high-income countries are still alive five years after diagnosis. This is also the case for the markets in this report, except for Thailand, which had a 5-year survival rate of less than 70% between 1995 and 2014; see Figure 2. There are also notable gaps between the high-income markets, even though improvements were observed in all markets in 1995–2014. Australia had the highest survival rate in the region, comparable to Japan. The gap between South Korea and Australia narrowed over the period, whereas both Hong Kong and Taiwan were persistently trailing Australia by around 8 percentage points.

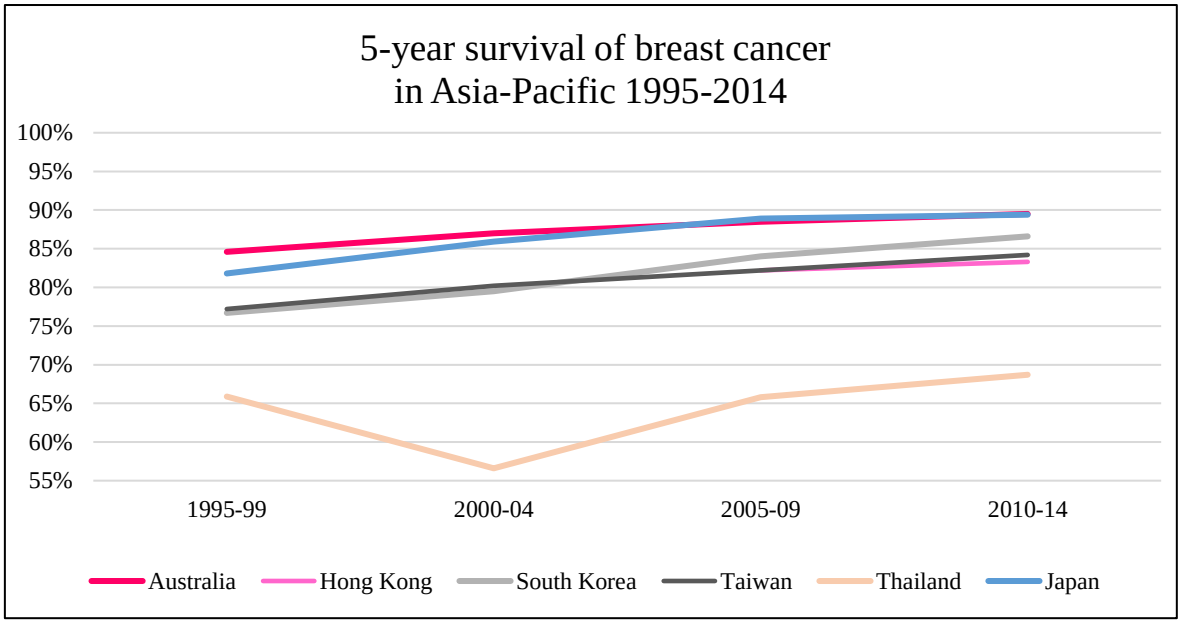

Figure 2: 5-year age-standardized relative survival of breast cancer in markets in Asia-Pacific and Japan in 1995–2014.

Notes: Hong Kong only includes data for 2005–2014. Data was gathered from regional registries that covered in 1995–99 and 2000–14 the following national population: 100% in Australia, Hong Kong, South Korea, and Taiwan, 20% in Thailand, and 41% in Japan. Source: CONCORD (8, 9).

Breast cancer is more common in younger women in Asia-Pacific than in Europe and Northern America; Figure 3. In South Korea, for instance, the median age at diagnosis is 52 years (10), which is 10 years younger than the median age in the United States (11). Figure 3 shows that more than half of all breast cancer cases are diagnosed in women between 45 and 64 years and almost one-fourth in women below the age of 45 in Asia-Pacific. The younger age distribution has negative consequences for the social and economic impact of breast cancer. Many women under 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.

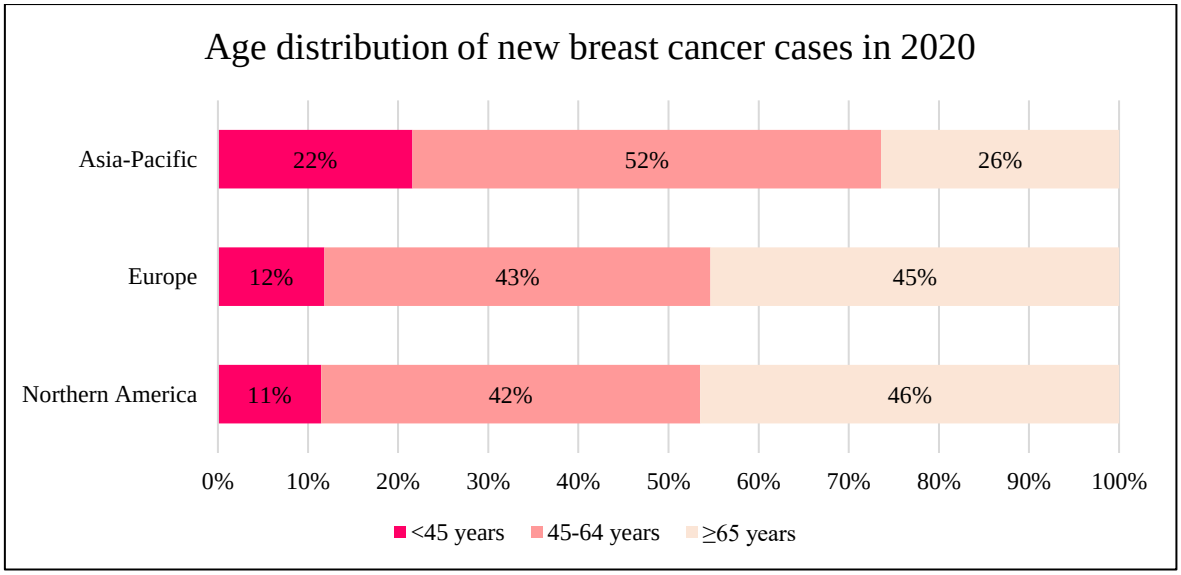

Figure 3: Age distribution of new breast cancer cases in 2020 by world region.
Notes: Asia-Pacific includes Asia and Oceania. Source: Estimates by IARC (2).

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 human epidermal growth factor receptor 2 (HER2) (12, 13); 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 (14). 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 (15). Systemic therapy options for TNBC have therefore been restrained to chemotherapy (16), 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 (17). Figure 4 shows that the prevalence of TNBC is between 9% and 13% in the selected Asia-Pacific markets. Except for South Korea, the figures are based on studies with comparatively small populations rather than population-based cancer registries. They should therefore be interpreted with caution.

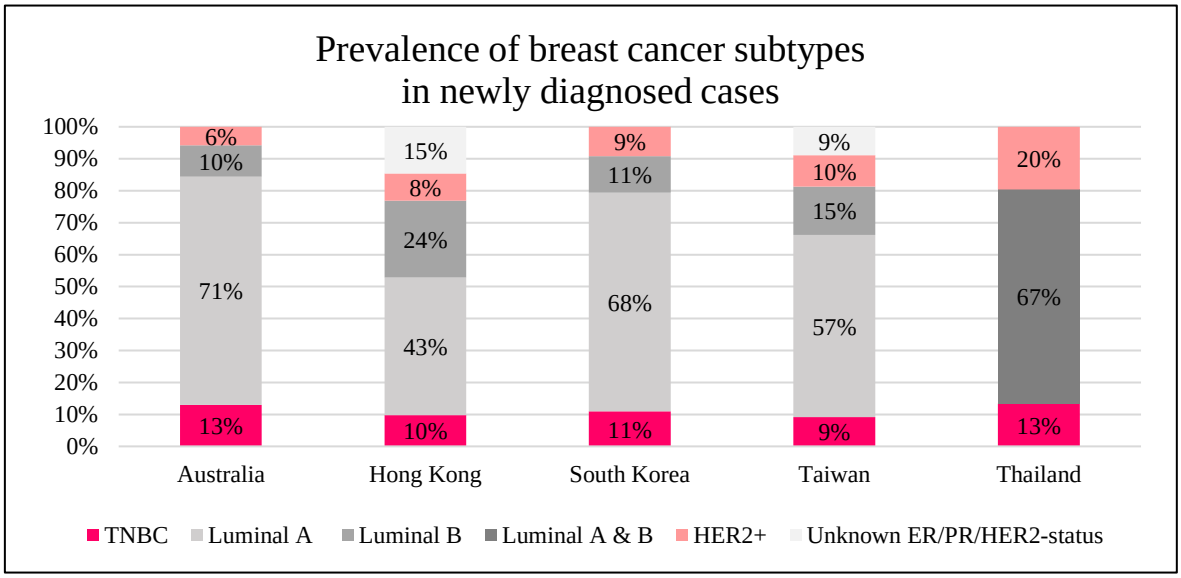

Figure 4: Prevalence of breast cancer subtypes in newly diagnosed cases in Asia-Pacific markets.

Notes: Australia shows data of diagnosed cases outside the screening program in Australia and New Zealand from 2005–2015 from the BreastSurgANZ Breast Quality Audit database. Hong Kong shows data from 2020 from the Hong Kong Cancer Registry. South Korea shows data from the Korean Breast Cancer Society registry from 2018. Taiwan shows data from the local cancer registry from 2019. Thailand shows combined data from the Khon Kaen University and Udonthani hospitals in Northeast Thailand from 2015–2020.
Source: (6, 18-21).

A key feature of TNBC is the younger age at diagnosis compared to other breast cancer subtypes (22, 23); see Figure 5. Young women with breast cancer may face consequences that affect them disproportionally 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 (24, 25). Figure 5 shows how the proportion of TNBC cases among women under 35 was higher than for the other subtypes.

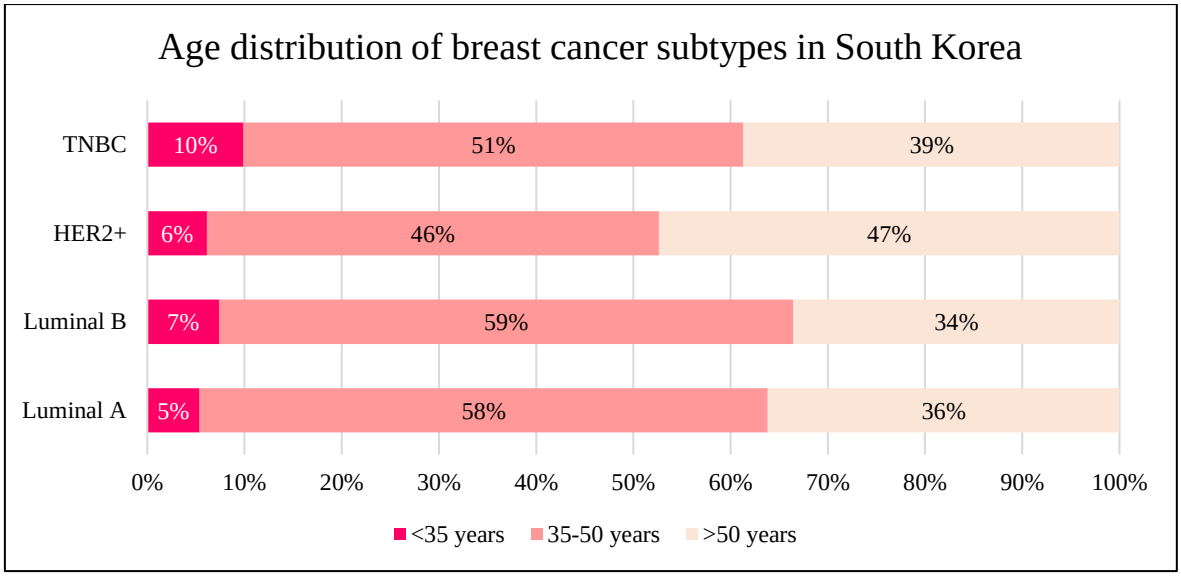

Figure 5: Age at diagnosis of breast cancer subtypes in South Korea.

Notes: Patients diagnosed with breast cancer registered in the Korean Breast Cancer Society Registry from 1993 to 2008 (n=61,375). Source: (26).

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). Studies in Thailand and Hong Kong have shown that TNBC diagnoses are less frequently diagnosed early in stage I compared to the other subtypes. For instance, 17% and 27% of TNBC cases in Northern Thailand and Hong Kong, respectively, were diagnosed in stage I (see Figure 6), whereas 33% and 87% of luminal A cases were diagnosed at stage I.

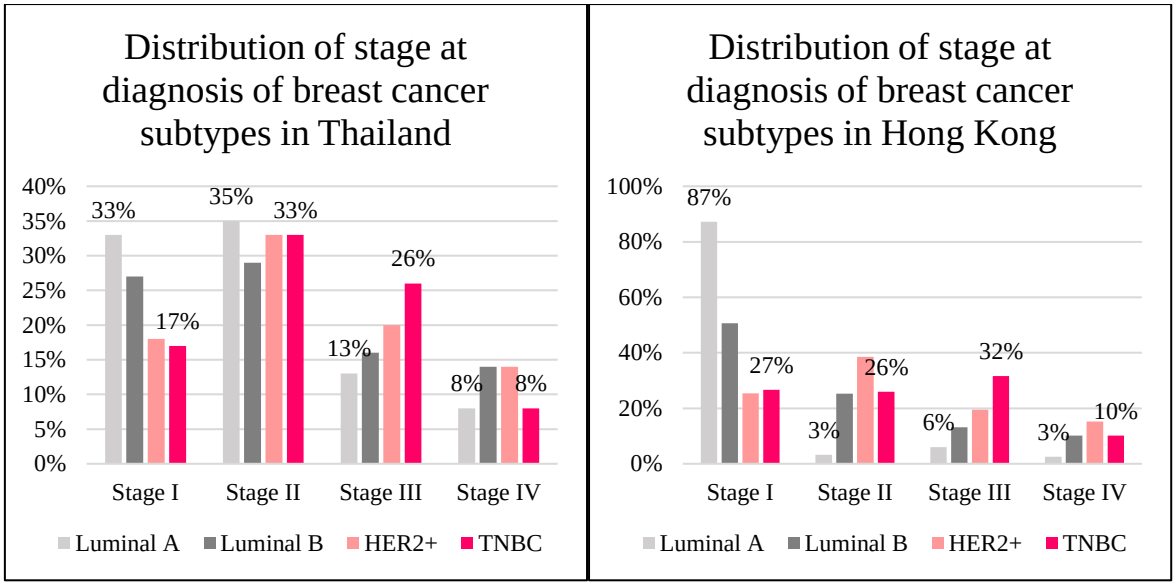

Figure 6: Stage at diagnosis of breast cancer subtypes in Northern Thailand and Hong Kong.

Notes: Data for Thailand come from the Chiang Mai Cancer Registry in Northern Thailand from diagnosed cases between 2006 and 2015 (n=3,251) and are thus not necessarily nationally representative. Data for Hong Kong come from the Hong Kong Cancer Registry in 2020 (n=4,956). Source: (19, 29).

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 summarized in Figure 7.

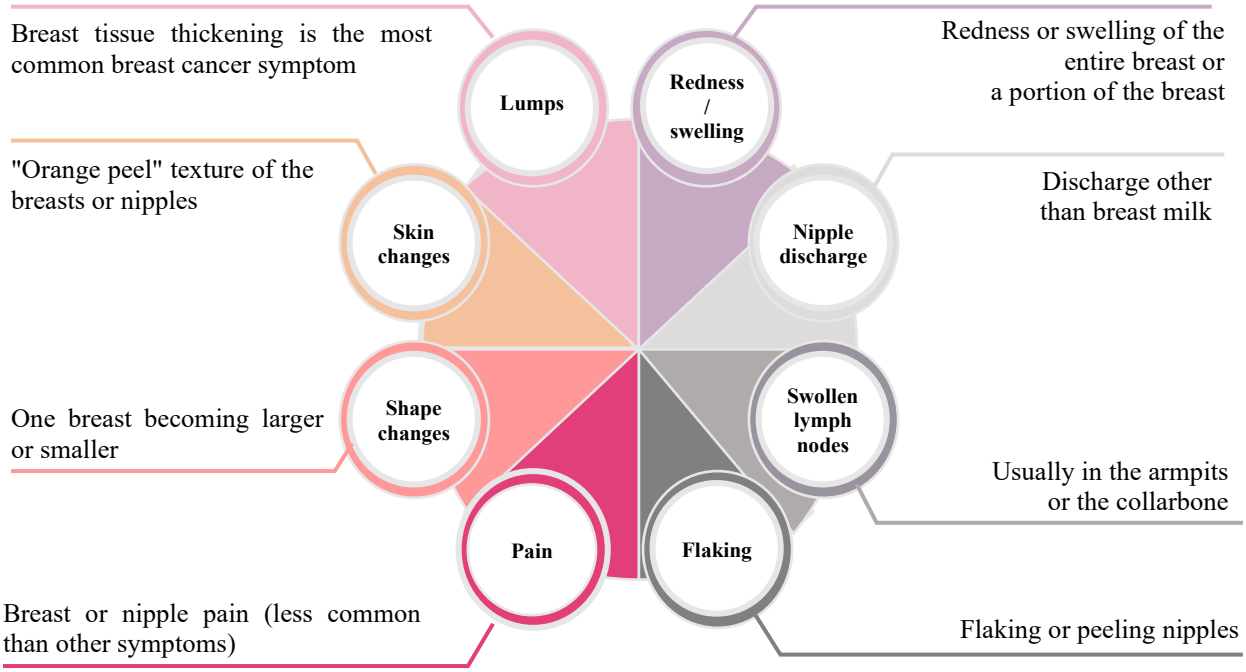

Figure 7: Common signs and symptoms of TNBC.

Source: (30).

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 Asia-Pacific
Age	The risk to develop breast cancer increases with age (31). This is also true for TNBC, but TNBC is more common in younger women than other subtypes (see section 1.2).	No specifics identified
Family history (Heredity)	Approximately 5–10% of all breast cancers have a hereditary background (32). The most common cause of hereditary breast cancer is an inherited mutation in the BRCA1 or BRCA2 gene (32). 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 (33). Women with BRCA1/2 have a particularly high risk to develop TNBC.	The estimated prevalence of BRCA1/2 mutations among breast cancer patients is around 8% in Hong Kong (34). A study from South Korea estimated that 13–14% of TNBC patients had a BRCA1/2 mutation (35). Another study from Australia estimated the prevalence of BRCA1/2 mutations in TNBC patients to be 9% (36).
Ethnicity	Black and Hispanic women are at an increased risk of developing TNBC compared to Caucasian women but reasons for this are unclear (37, 38). In the United States, black women are nearly three times more likely than Caucasian women to be diagnosed with TNBC (39).	Asian women in the United States had a lower absolute lifetime risk of developing TNBC than Black, Hispanic, and Caucasian women (40). A study examining how breast cancer subtypes differ by Asian ethnic groups in the United States found that Korean women had a higher proportion of TNBC than Filipino, Japanese, or Chinese women (41).
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 (42). The link between breast density and developing TNBC is stronger in premenopausal women than in postmenopausal women (39).	Studies have shown that Asian women are more likely to have dense breasts (43). In Taiwan, around 80% of mammograms in women under 55 and 59% in women aged 60–64 are classified as extremely dense (44). In South Korea it is estimated that more than half of women aged 40–69 have dense breasts (45).

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 Queensland, Australia estimated that 26% of all invasive breast cancers were attributed to modifiable risk factors (46); see Figure 8. The largest modifiable risk factor was obesity/overweight, which was attributable to 12% of all breast cancer cases, followed by physical inactivity (8% of all breast cancer cases).

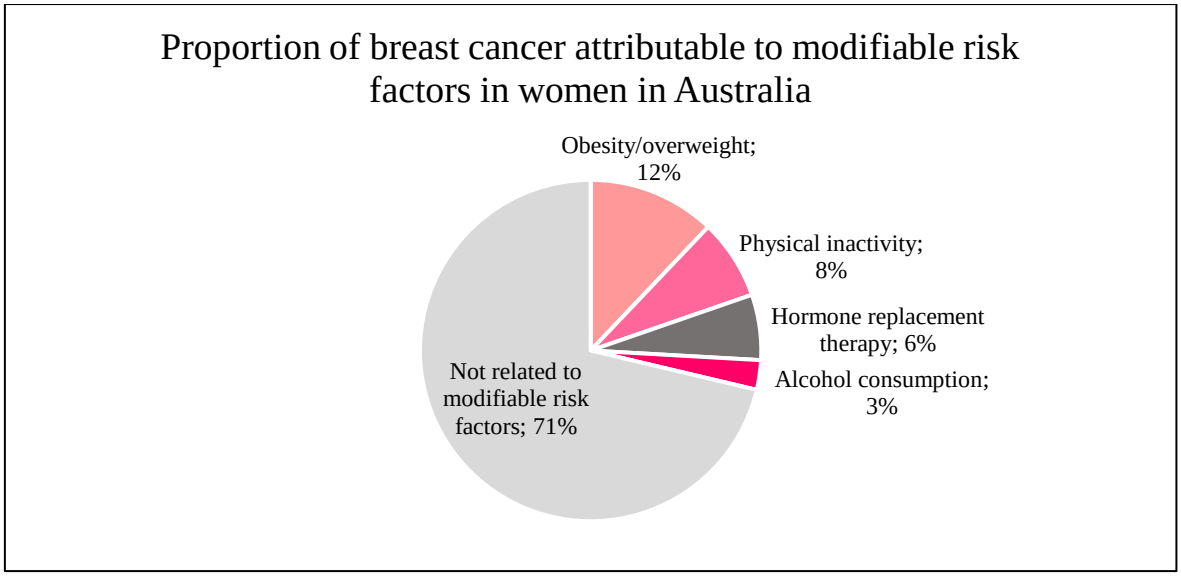

Figure 8: Proportion of breast cancer attributable to modifiable risk factors in women aged 45–69 years in Queensland, Australia.

Notes: The individual sum of the proportions of the four risk factors is 29% whereas the overall proportion attributable to these risk factors is 26% when simultaneously controlling for the mutual association between risk factors. Source: (46).

Figure 9 shows the prevalence of the most common risk factors identified in breast cancer patients in Hong Kong in the period 2006–2018 (47). The most prevalent risk factor was physical inactivity, with 78% of the patients reporting that they exercised less than 3 hours per week. They were followed by not breastfeeding and overweight/obesity with a prevalence of 66% and 39%, respectively.

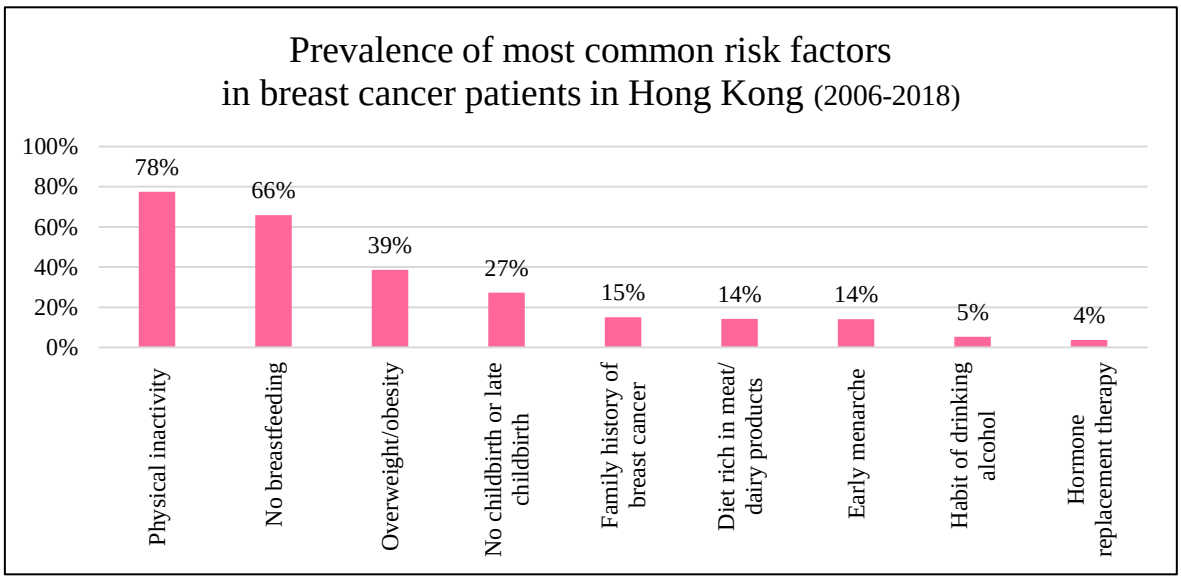

Figure 9: Prevalence of top 10 most common risk factors in breast cancer patients in Hong Kong (2006–2018).

Notes: The Hong Kong Breast Cancer Registry gathered data from all breast cancer cases diagnosed from 2006 to 2018 (n=21,866). Not all included risk factors have a high-level of evidence of a link to breast cancer. Source: (47).

Table 3: Modifiable risk factors in TNBC

Risk factor	Description	Specifics for Asia-Pacific
Obesity and overweight	Obesity has been linked with a higher likelihood of developing TNBC (48). For breast cancer overall, the link seems to be stronger in postmenopausal women than in premenopausal women (49).	Obesity rates in Asia-Pacific have been increasing steadily since 1975; see Figure 10. In 2016, the prevalence of obesity among women in Australia was 29.5%, in Hong Kong 10.7%, in South Korea 5.0%, in Taiwan 8.6%, and in Thailand 13.2% (50).
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 (51).	The markets with the highest prevalence of female physical inactivity are South Korea (43%) and Australia (35%); see Figure 11. These markets have a higher prevalence of physical inactivity than the average in Europe (32.4%) (52).
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 (53).	In the region, Thailand has low breastfeeding rates. It is estimated that only 23% of babies are breastfeed for six months while the global WHO target is 50% (54).
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 (55). 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 specifics identified

Notes: Alcohol consumption (56), cigarette smoking (57), hormonal replacement therapy to treat menopausal symptoms (58), and use of oral contraceptives (59) 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 (60, 61).

A 2014 survey in Thailand found that Thai women had a high level of unawareness of risk factors of breast cancer. Only 5% of women knew that the lack of physical activity had a link to breast cancer and 4% that being overweight increased the risk of getting breast cancer (62).

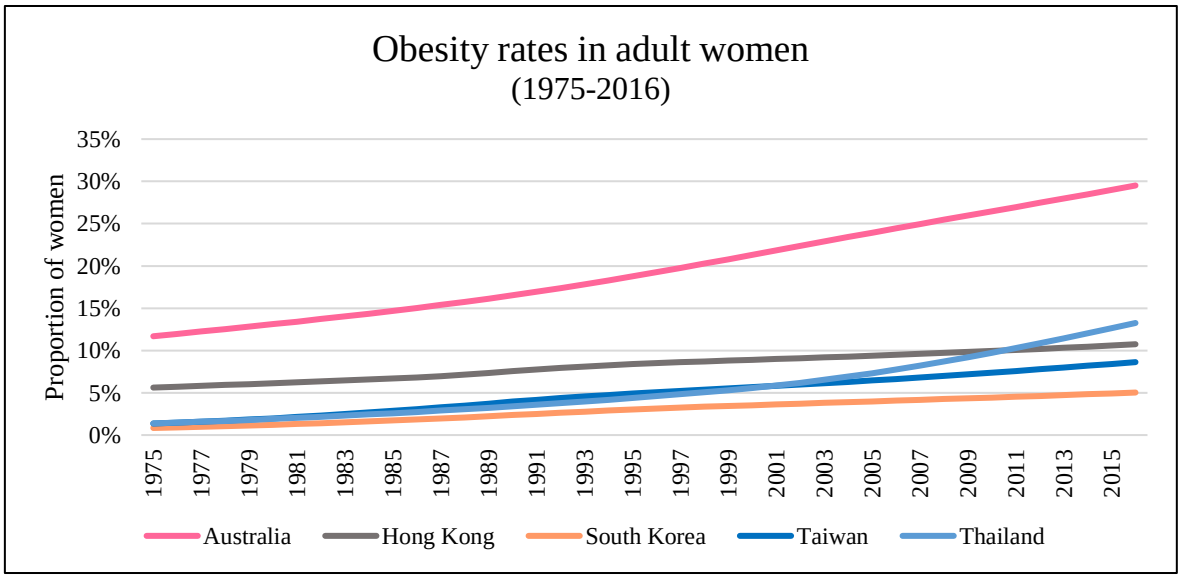

Figure 10: Prevalence of obesity in adult women in Asia-Pacific, 1975–2016.

Notes: Obesity is defined as BMI ≥ 30. Age group ≥ 18 years. Source: (50).

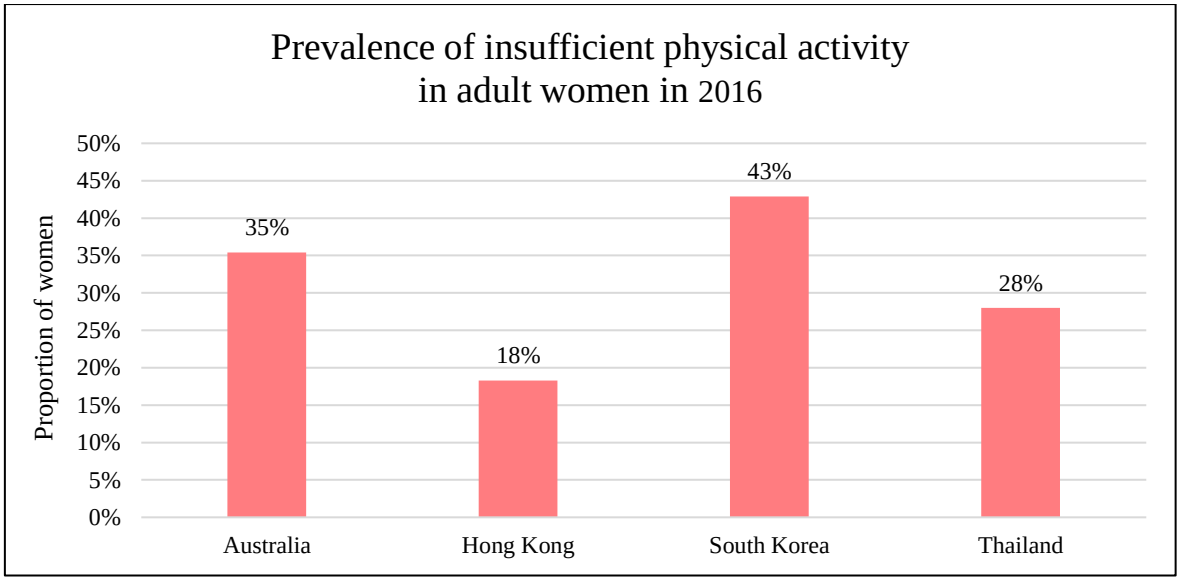

Figure 11: Prevalence of insufficient physical activity in adult women in Asia-Pacific.

Notes: Age group ≥ 18 years. Hong Kong data was gathered from the Health Behavior Survey 2018/19. For the rest of the markets the rates refer to 2016. Source: WHO (52), Health Behavior Survey Hong Kong (63).

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 geographic region. High-income markets in Asia-Pacific have population-based cancer registries that collect and provide information on annual breast cancer incidence and mortality. Thailand only has regional population-based cancer registries that integrate information available on annual breast cancer incidence, covering approximately 31% of the population in 2019 (64). However, information on the annual incidence of TNBC is absent in all markets, 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. Similarly, information on the number of TNBC deaths is generally absent.

Overall, the estimated incidence rate of breast cancer in Asia-Pacific increased from 37 cases per 100,000 women in 1995 to 93 cases per 100,000 women in 2020; see Figure 12. The estimated increase for this period was 149% for the weighted average in the region (excluding Thailand which lacks a national population-based cancer registry). During the same period, the estimated mortality rate of breast cancer increased by 49%. The lower relative increase in mortality compared to incidence is a sign of progress in breast cancer over this period.

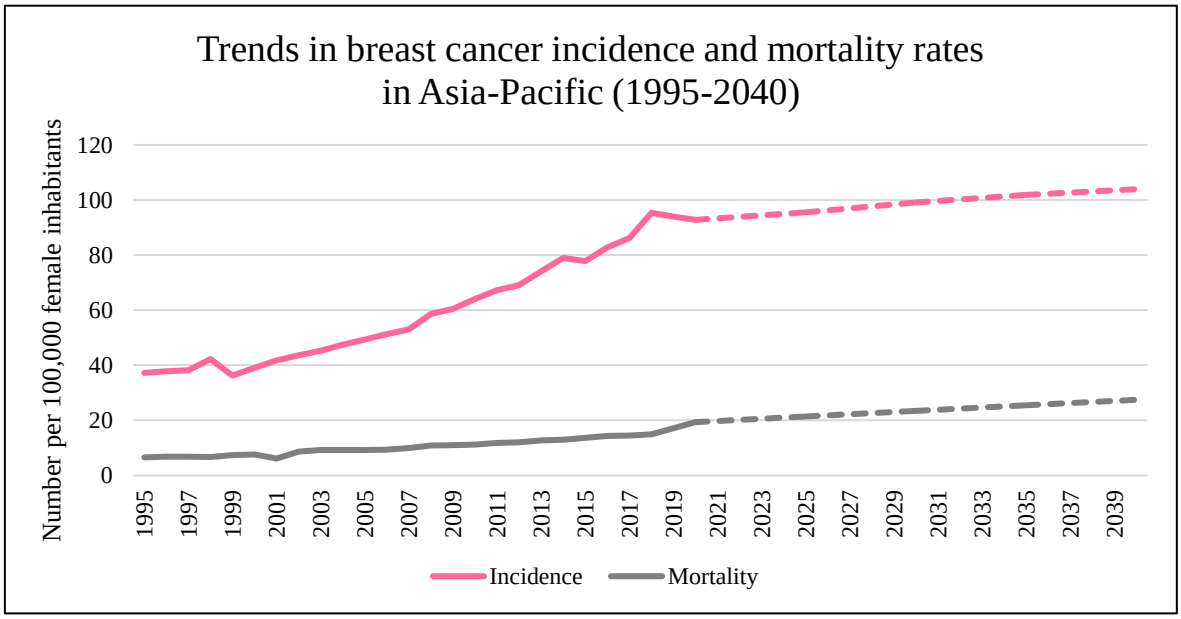

Figure 12: Estimated trends in breast cancer incidence and mortality crude rates per 100,000 female inhabitants in Asia-Pacific, 1995–2040.

Notes: The numbers are the population-weighted averages of Australia, Hong Kong, South Korea, Taiwan, and Thailand. Numbers between 2020 and 2040 are predictions based on unchanged age-specific risks to get

and die from breast cancer for Australia, South Korea, and Thailand. Due to unavailable data, crude breast incidence rates in Thailand were imputed for 2013–2019. Source: (65-68).

The incidence of breast cancer has not just been increasing in the past in Asia-Pacific, but it is also predicted to continue to increase in the future. Figure 12 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 12.

Figure 13 shows breast cancer incidence and mortality rates in the individual Asia-Pacific markets in 2020. The market with the highest incidence was Australia, with an estimated 153 cases per 100,000 women. Thailand had the lowest incidence with 62 cases per 100,000 women. The mortality rates in Australia and Thailand were almost identical at 24 and 23 cases per 100,000 women, respectively. The much bigger gap between incidence and mortality in Australia compared to Thailand is reflective of the distinctly lower survival of Thai breast cancer patients (see also section 1.1).

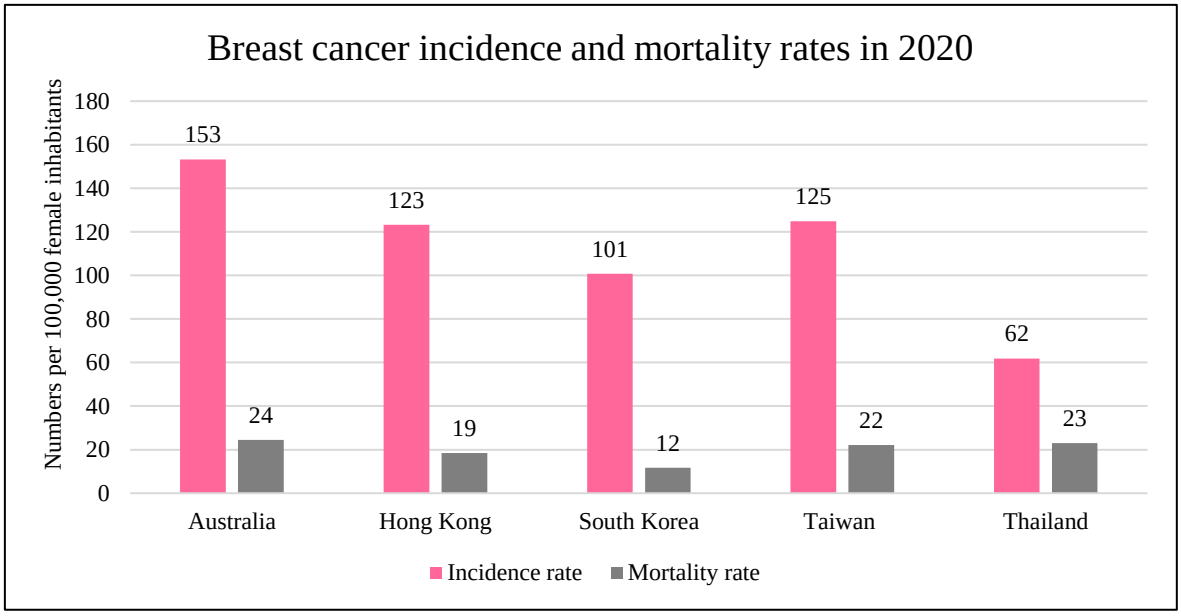

Figure 13: Breast cancer incidence and mortality crude rates per 100,000 female inhabitants in 2020.

Sources: Estimates for Australia, South Korea, and Thailand by IARC (2). Data from Hong Kong are from the Hong Kong Cancer Registry (HKCR) (5). Data from Taiwan are from 2019 and were retrieved from the Taiwan Cancer Registry Center (TCRC) (67).

[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.

2.2 Survival

Survival is a key measure of the disease burden of a cancer type for the individual patient. It measures the likelihood of being alive X years after diagnosis. In the absence of population-based cancer registries that track data by molecular subtypes, data on the survival of patients with TNBC that distinguishes them from other breast cancer subtypes are scarce.

The data points for survival of TNBC patients are summarized in the following graphs for each market, with differing data periods, sample sizes, and clinical characteristics of the patients covered, thus restricting their comparability. Nonetheless, all studies consistently show that:

- TNBC has the lowest survival rate of all breast cancer subtypes; see Figure 14 to Figure 17.
- The survival rate of TNBC is lower than non-TNBC at each stage at diagnosis, such as in Taiwan (Figure 14), Hong Kong (Figure 15) and Australia (Figure 17).
- The likelihood of survival is significantly influenced by the stage at diagnosis. The earlier the diagnosis, the better the prognosis. For instance, Figure 14 shows for Taiwan that the 5-year survival rate at stage I TNBC was 95% but dropped to 11% in stage IV when the tumor was metastasized at the time of diagnosis.

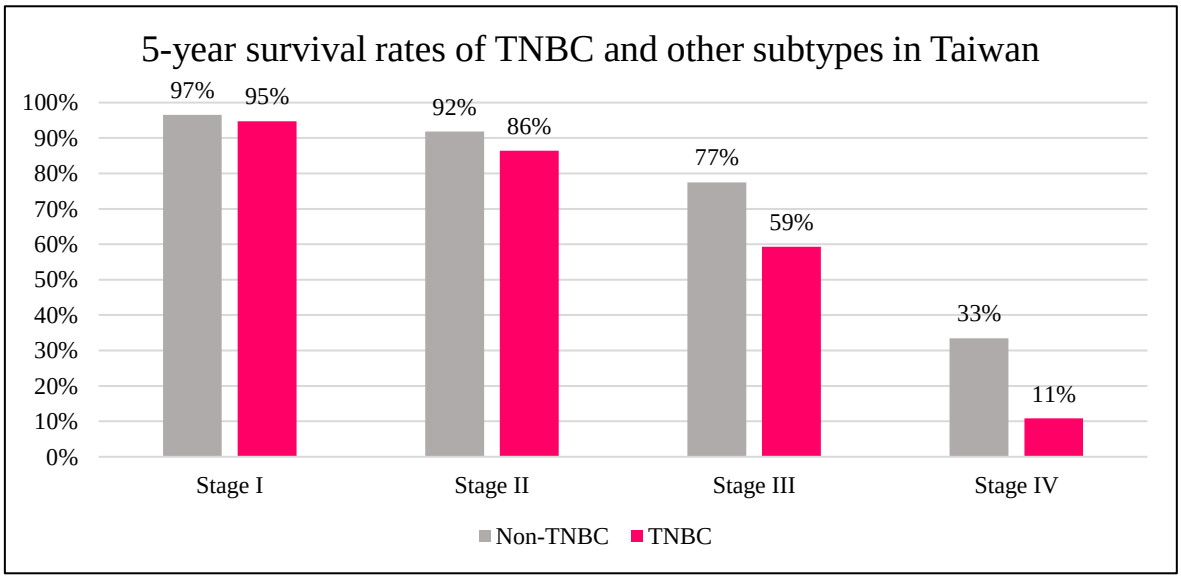

Figure 14: 5-year absolute survival rates of TNBC and non-TNBC breast cancer in Taiwan.

Note: N = 50,856 breast cancer cases retrieved from the Cancer Registry database and the Death Registry database in 2008–2013. Source (69).

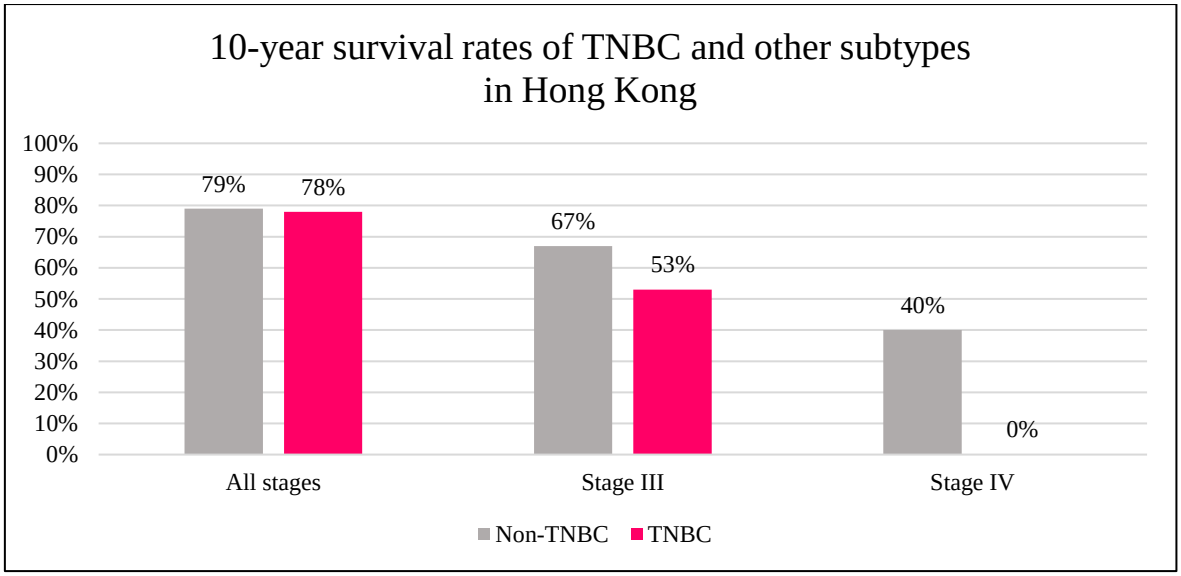

Figure 15: 10-year absolute survival rates of TNBC and non-TNBC patients in Hong Kong.

Notes: N = 1,800 breast cancer cases from a tertiary referral unit in Hong Kong in 1995–2006. Source: (70).

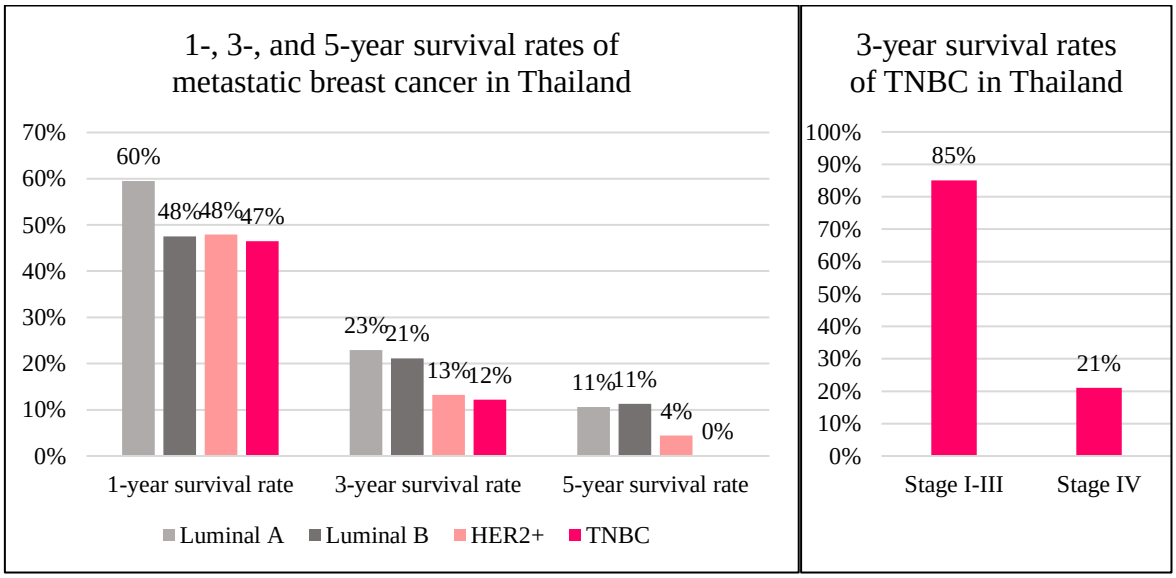

Figure 16: 1-, 3-, and 5-year absolute survival rates of metastatic breast cancer patients (left graph) and 3-year absolute survival rate of TNBC patients by stage at diagnosis (right graph) in Thailand.

Notes: Data for the right graph come from the Rajavithi Hospital comprising cases from 2005–2013 (n=232). Data for the left graph come from a national multi-center study comprising cases from 2011–2016 (n=293). Source: (71, 72).

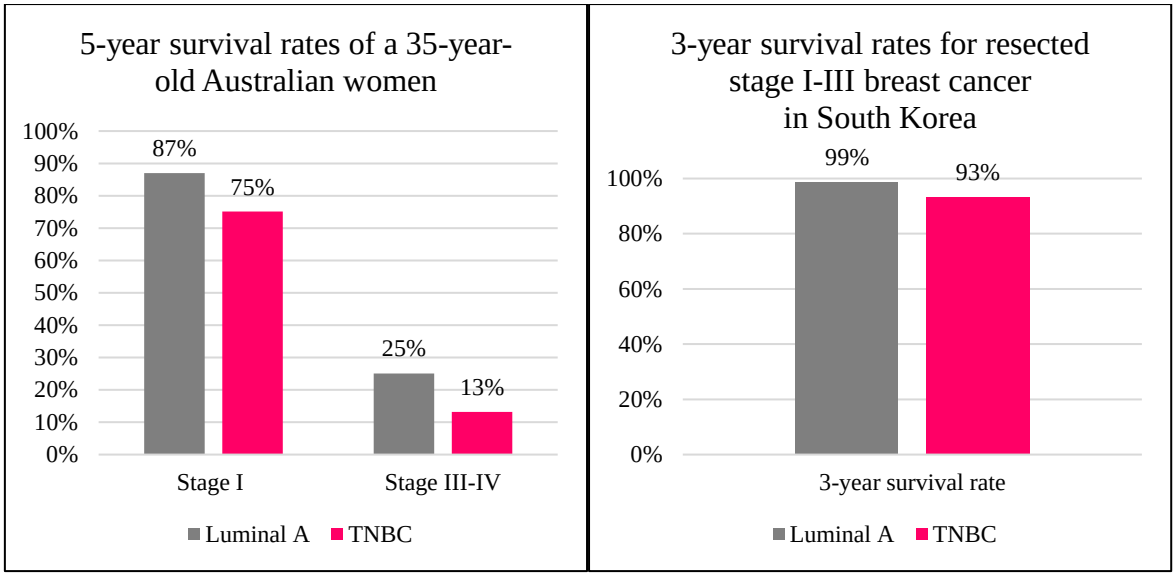

Figure 17: 5-year survival rates of a hypothetical 35-year-old breast cancer patient in Queensland, Australia and 3-year survival rates of resected stage I–III breast cancer patients in South Korea.

Notes: Australian data was gathered from a prognostic model that estimated relative survival rates with information from women diagnosed with breast cancer in Queensland in 2010–2013 (n=3,323). South Korean data show absolute survival rates and comprise cases registered in the Korean Breast Cancer Society Registry from 1993–2008 (n=61,375). Source: (26, 73).

A contributing factor to the comparatively low survival rate of TNBC is its tendency to recur (i.e., come back) after initial treatment (74). For example, data from Canada show that almost 40% of non-metastatic TNBC patients diagnosed in 2004–2012 experienced recurrence while fewer than 10% of luminal A patients did (75).

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 (76); 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.

Figure 18 presents the findings of a study for South Korea that estimated the direct and indirect costs of breast cancer (77). The direct and indirect costs were equally large. The high contribution of indirect costs is explained in part by the young age at which breast cancer is diagnosed, affecting many working-age patients.

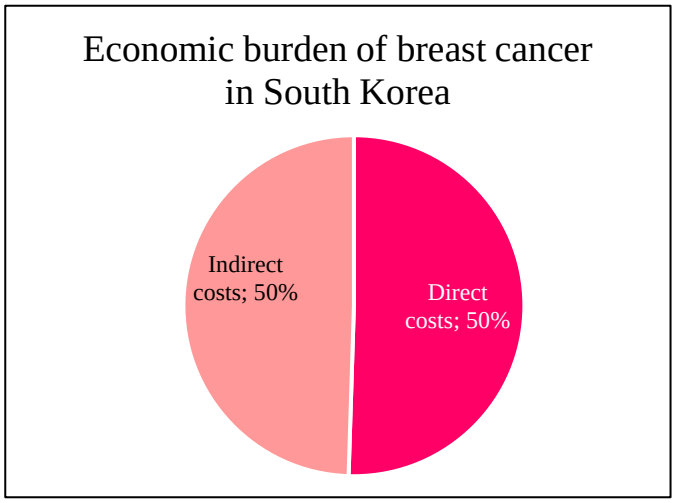

Figure 18: Economic burden of breast cancer in South Korea in 2010.

Notes: Data was collected from the Korea National Health Insurance (KNHI) and the Korean National Statistical Office. Direct costs include medical costs (medical services paid for by insurance, copayments, non-covered services, medicines) and non-medical costs (transportation, time spent by caregivers). Indirect costs include lost productivity due to being sick and premature death. Source: (77).

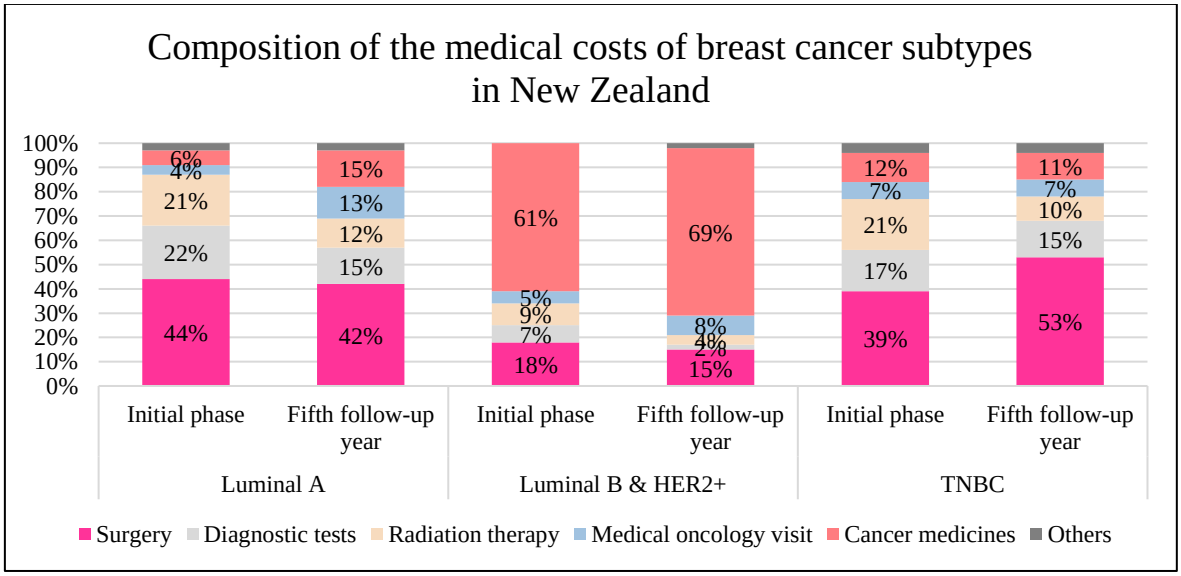

Figure 19: Composition of the medical costs of breast cancer subtypes in by treatment year in New Zealand.

Notes: The "initial phase" covers 3 months preceding and 12 months following diagnosis of breast cancer, and "fifth follow-up year" is the fifth year after diagnosis of breast cancer. Data come from the National Breast Cancer Register and the New Zealand Cancer Registry from breast cancer patients diagnosed in 2010 to 2018 treated in the public sector (n=22,948). Source: (78).

The direct medical costs of breast cancer are composed of the costs of various services received throughout the patient journey. Figure 19 shows the distribution of costs for patients with different subtypes of breast cancer in New Zealand in 2010–2018 (in absence of any other study in the Asia-Pacific markets in this report). Costs for surgery accounted for around 40% of the total costs for luminal A and TNBC in the initial phase of the treatment but also subsequently, whereas costs of

cancer medicines only accounted for 6–15% in luminal A and 11–12% in TNBC. In contrast, in patients with a positive expression of HER2 (luminal B and HER2+) cancer medicines accounted for around two thirds of the total costs, driven by the use of HER2-directed targeted therapy.

Breast cancer patients may also incur out-of-pocket (OOP) expenses to pay for direct costs that are only partially funded by public payers. Apart from copayments on medical services, patients may also have to pay for transportation, fertility treatments, or mental health care services. In Australia, where public health care is provided to all citizens, 86% of breast cancer patients reported incurring OOP expenses (79). The median medical and non-medical OOP expenses were $4,809 in the first five years following diagnosis in a study of 1,919 Australian breast cancer patients (79). This included OOP expenses such as for medical consultations, tests, and treatments, travel and accommodation.

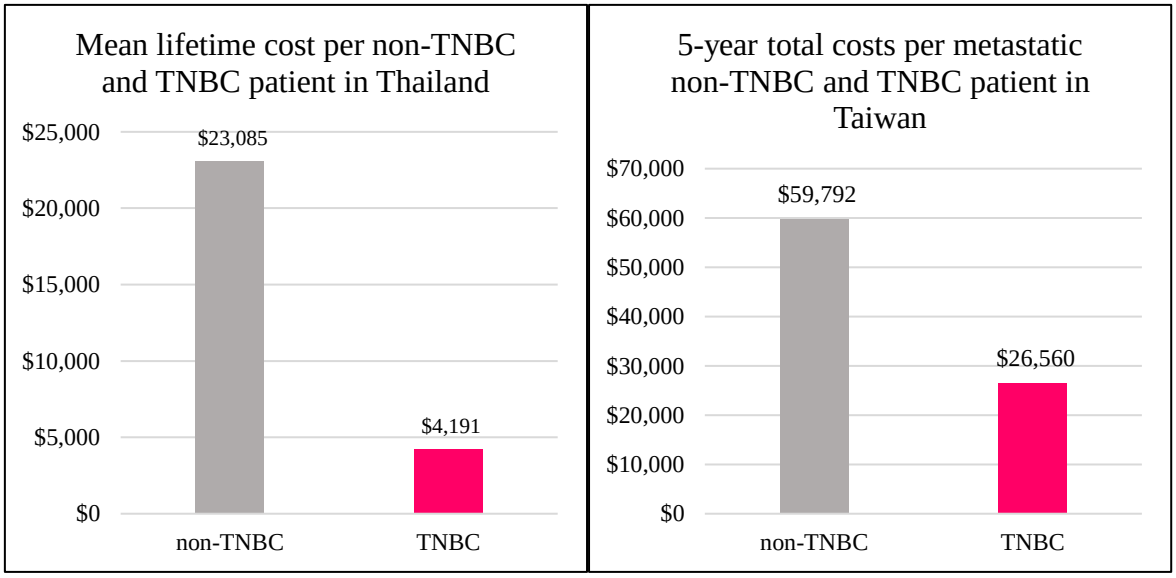

Figure 20: Mean lifetime cost of TNBC and non-TNBC patients in Thailand and 5-year total costs of metastatic TNBC vs. metastatic non-TNBC patients in Taiwan (in US dollars).
Source: (69, 80).

Some studies in the Asia-Pacific region have compared the direct medical costs of TNBC to other breast cancer subtypes. The general finding is that the costs of TNBC are lower than of other subtypes. In Thailand, the mean lifetime medical costs of TNBC patients ($4,191) was significantly lower than the ones for non-TNBC patients ($23,085) (80); see Figure 20. Medicines accounted for 76% of the mean lifetime costs for TNBC patients and 87% for non-TNBC patients in Thailand. A study of metastatic breast cancer patients in Taiwan found that TNBC had lower 5-year total costs ($26,560) than non-TNBC patients ($59,792) (69); see Figure 20. The largest cost component in these metastatic patients with non-TNBC and TNBC was hospitalizations in Taiwan. Similarly, in New Zealand the median public per-patient health care costs of TNBC were the second lowest (NZD 31,722) after luminal A (NZD 28,481) whereas HER2+ (including luminal B) had more than three

times higher costs (NZD 106,428) (78). Over half of the costs for HER2+ breast cancers were medicines costs for targeted therapy, whereas surgery and radiation therapy incurred the biggest costs in the other subtypes.

The direct medical costs of breast cancer generally increase considerably in advanced stages due to more complex and intensive treatments. Costs of TNBC divided by stage in the Asia-Pacific markets in this report are lacking. However, a study from New Zealand showed that median costs per patient diagnosed in stage IV were 2.5 times higher than the ones for patients diagnosed in stage I over a five-year period; see Figure 21. A recent review of studies from high-income countries outside of the Asia-Pacific region also found that annualized per-patient direct medical costs ranged from around $20,000–100,000 in early-stage TNBC (stage I–III) to around $100,000–300,000 in metastatic TNBC (stage IV) (81). 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 some Asia-Pacific markets (see section 3.2), would not only save lives but also health care costs.

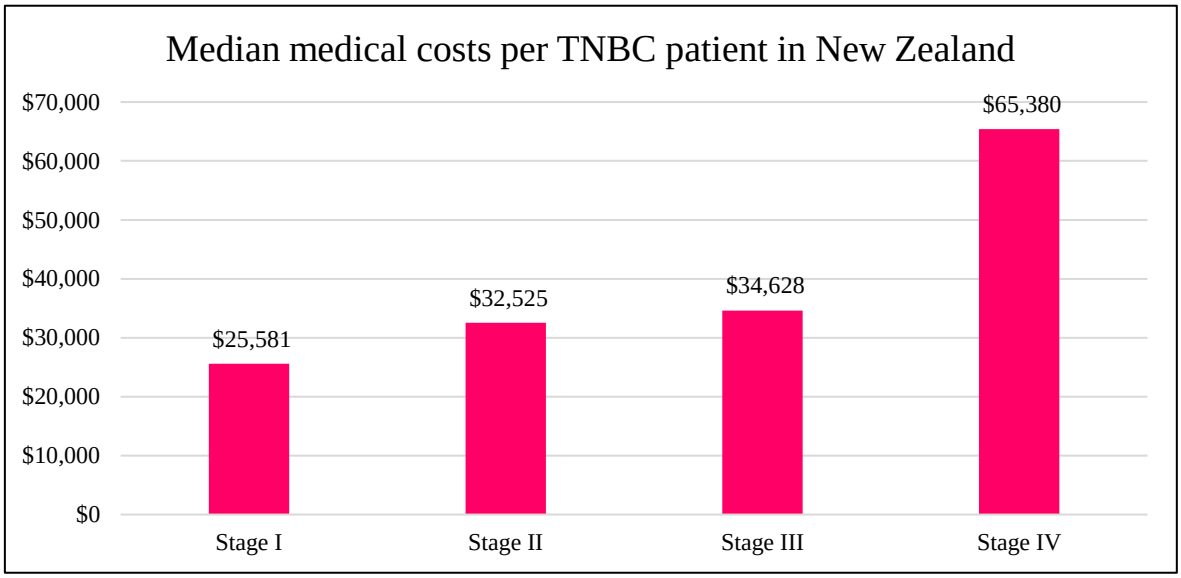

Figure 21: Median medical costs per TNBC patient in the first five years after diagnosis in New Zealand by stage of disease at diagnosis (in NZ$ year 2019/2020).

Notes: Data come from the National Breast Cancer Register and the New Zealand Cancer Registry from TNBC patients diagnosed in 2010–2018 treated in the public sector (n=22,948). Source: (78).

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 22. 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).

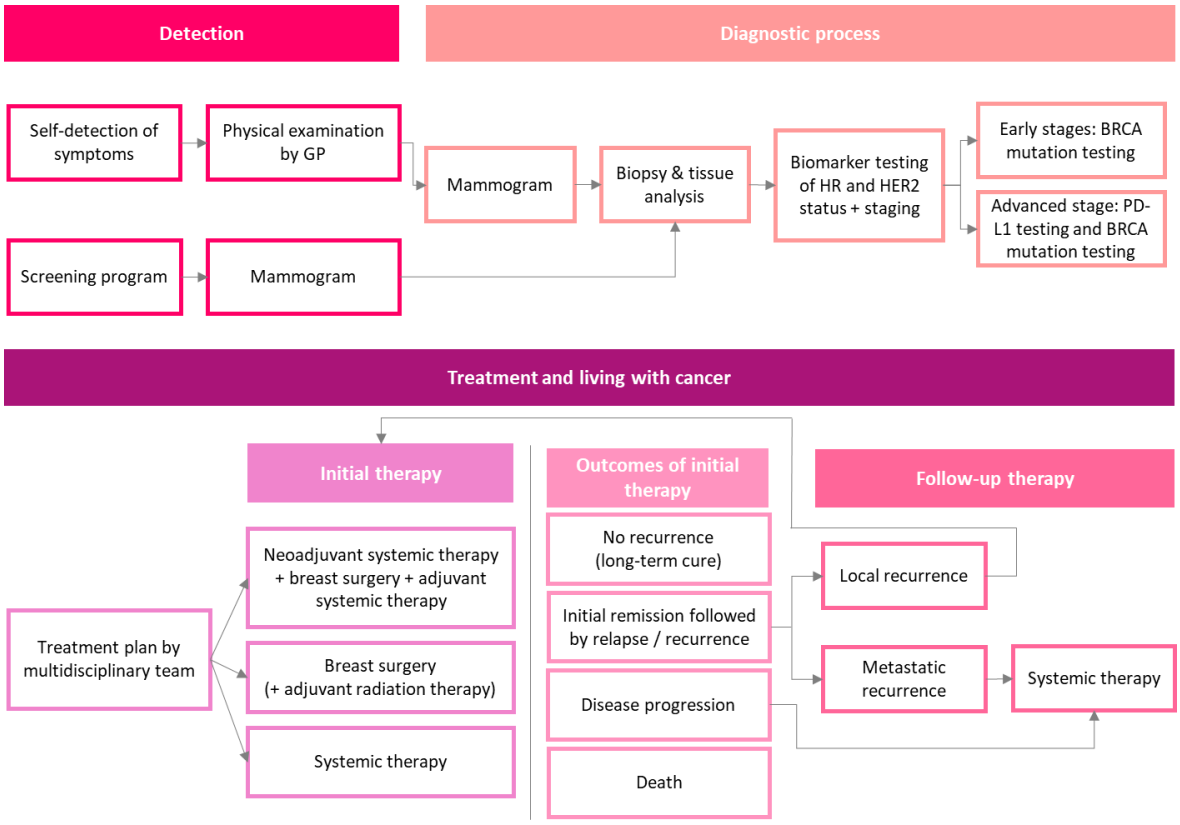

Figure 22: Stylized patient journey in TNBC.
Notes: Based on American Cancer Society and ASCO, ESMO, and NCCN guidelines (82-85).

In 2021, the WHO launched the Global Breast Cancer Initiative to enhance the quality of breast cancer care, particularly in low- and middle-income countries (86). The initiative aims to decrease the global breast cancer mortality rate by 2.5% annually and prevent 2.5 million breast cancer deaths from 2020 to 2040. The initiative consists of three aims which correspond to the key stages depicted in Figure 22.

1. Health promotion for early detection (pre-diagnostic interval)
    - KPI: >60% of cancer cases are stage I or II at diagnosis.
2. Timely breast 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 an in-depth look at the health systems in the markets under study and elaborate on some of the most significant obstacles faced in each of these three domains.

3.1 Health system readiness

The Asia-Pacific markets under study have performed quite well on a set of fundamental health indicators (87). Universal Health Coverage (UHC), for instance, has been achieved in all markets. According to the WHO index of essential service coverage, coverage ranged from 87 points (out of 100) in Australia, Hong Kong, and South Korea to 83 in Thailand (88). These numbers indicate acceptable levels of health care access and utilization, comparable to Western high-income countries. However, there are still persistent challenges in ensuring health care access to everyone as marginalized groups struggle with practical impediments to access services that are further described in section 3.2. Moreover, the growing demand for health care due to population aging adds additional pressure on the health care systems.

The monetary resources invested in health care differ across Asia-Pacific markets. Australia spends close to 10% of its gross domestic product (GDP) on health care, while Thailand spends just below 4%; see Figure 23. In addition, the public part of the total health expenditure falls below the informal WHO public spending target of 5% of GDP in Hong Kong (3%), Thailand (3%), and Taiwan (4%), while South Korea just meets the target. In absolute numbers, Australia spends the most on health care with almost $5500 per capita, compared to $3000 in Hong Kong, $2600 in South Korea, $1600 in Taiwan, and $300 in Thailand.

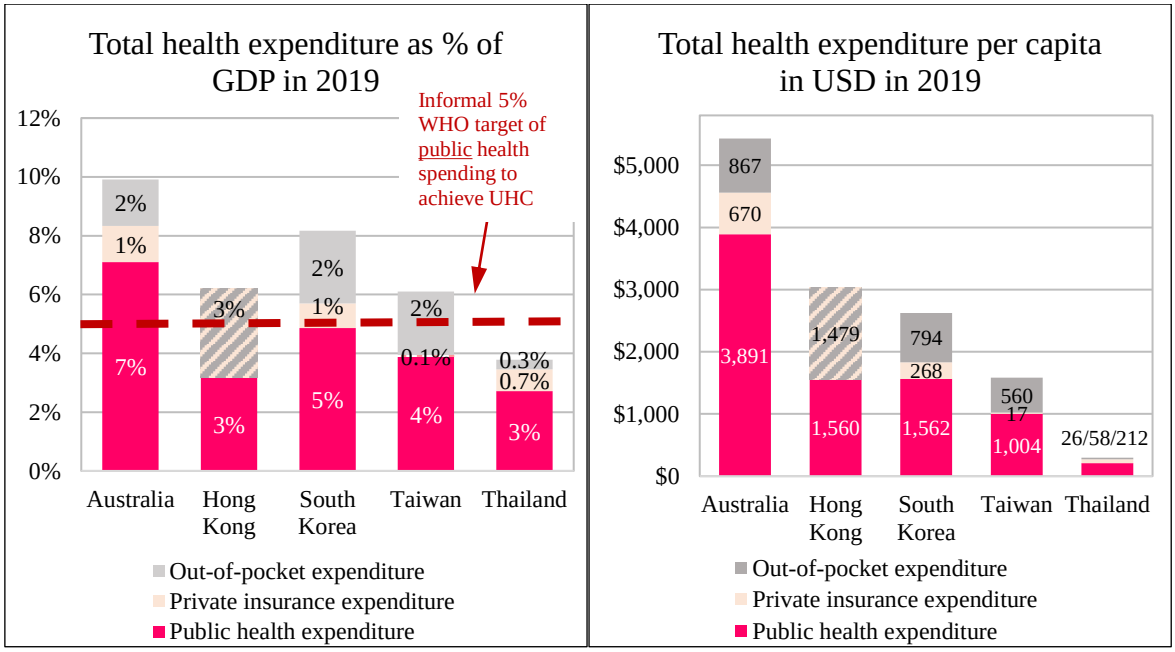

Figure 23: Total health expenditure as percentage of GDP and in USD per capita in 2019.

Notes: GDP = gross domestic product. Expenditure is not adjusted for differences in purchasing power parity. Hatched bars indicate no distinction between out-of-pocket expenditure and private insurance expenditure. Source: WHO (89), Department of Health for Hong Kong (90), Ministry of Health and Welfare for Taiwan (91).

Differences in health spending on cancer care in the region have been previously described. The proportion of the total health spending on cancer care ranged from 9.1% in South Korea in 2009, to 4.5% in Australia in 2013 to about 2.1% in Thailand in 2018 (92). In comparison, in Japan it was estimated to be 7.5% and the average in Europe was 6% of total health expenditure in 2018 (92).

The health care systems in the Asia-Pacific markets under study are dominated by the public sector; see Figure 24. In Australia, Hong Kong, South Korea, and Taiwan, the entire population is covered by a single public health insurance. The fact that the public system provides the majority of health care services in these markets poses some challenges. In Hong Kong, it has resulted in overcrowded public health facilities and lack of health care staff in the public sector (93).

In contrast, public health care in Thailand is divided into a social security scheme (SSS) for private formal sector employees, a scheme that provides health care to government officials (CSMBS), and one for the rest of the population (UCS). Each of these schemes has a unique funding structure and allocates its resources differently. The fragmentation of the health systems poses two challenges for the treatment of breast cancer. First, the effectiveness of national breast cancer prevention initiatives is undermined. Second, there are profound inequalities in the range of health services available in each scheme.

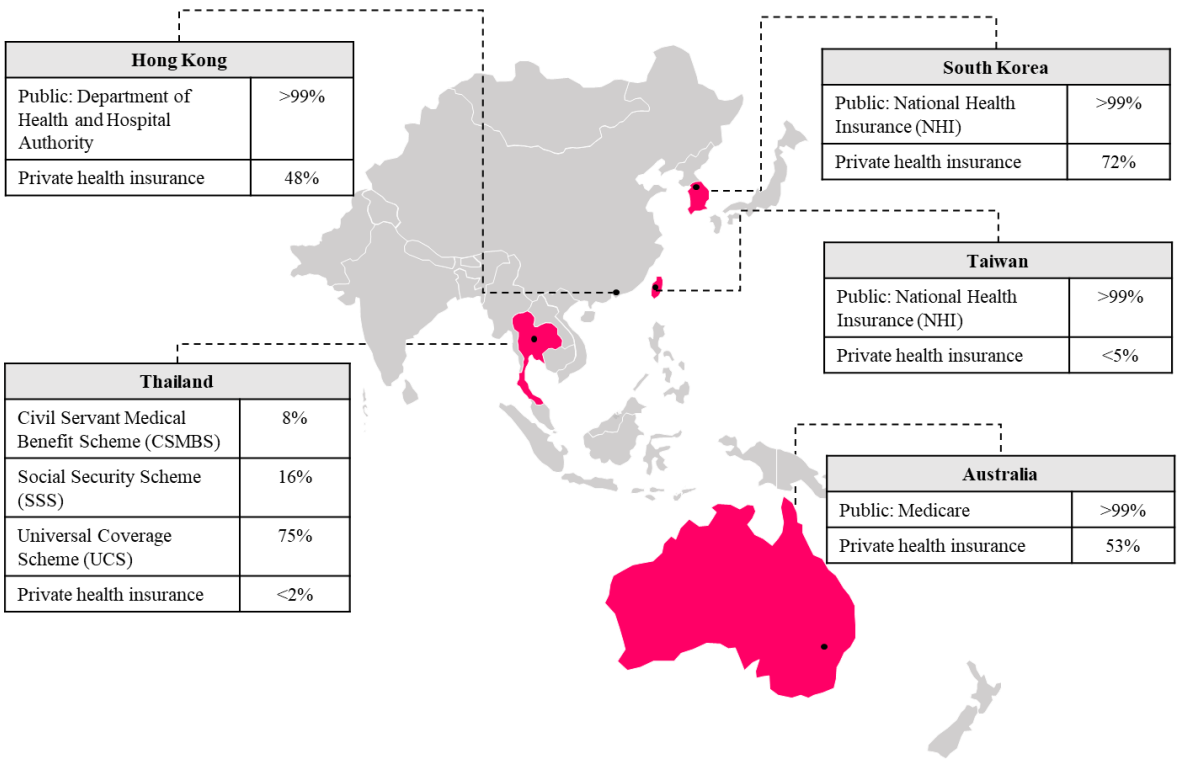

Figure 24: Health insurance coverage (% of population covered) in Asia-Pacific.
Source: Australia (94), Hong Kong (93), South Korea (95, 96), Taiwan (97), Thailand (98).

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.

Self-detection is still a key method for breast cancer detection in Asia-Pacific, even in countries with free population-based screening programs as the target age bracket of these programs is restricted. For instance, it is estimated that around half of all new breast cancer cases in Australia are self-detected despite the availability of a screening program (99).

The data shown in Figure 25 reflects the rate of early diagnosis of breast cancer at stages I and II and the goal set by the WHO's Global Breast Cancer Initiative of 60% (86). It is encouraging to note that all markets analyzed have achieved this target, except for Thailand, where it is estimated that 55% of diagnoses occur at these early stages.

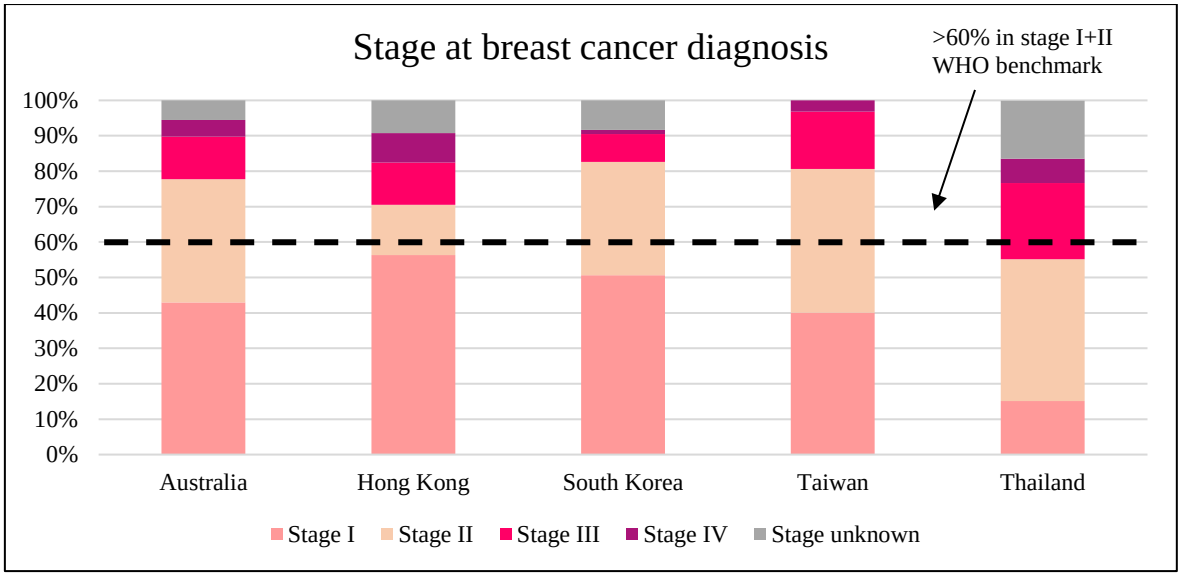

Figure 25: Stage distribution of breast cancer at diagnosis and WHO target.

Notes: Data for Australia include all diagnosed cases in 2011 (n=14,215). Data for Hong Kong and South Korea include newly diagnosed cases in 2018 (n=5,287) and (n=28,157), respectively, and data were extrapolated excluding stage 0. Data for Taiwan include patients diagnosed in 2011–2017 (n=49,426). Data for Thailand include patients diagnosed in the Maharaj Nakorn Chiang Mai Hospital in 2006–2015 (n=3,868). Sources: (10, 47, 100-102).

Despite the progress made in early detection, all markets still have room for improvement. Figure 26 depicts key challenges in early breast cancer detection. Although these challenges may not affect each market equally, they are present in at least one of them. A detailed description is provided below.

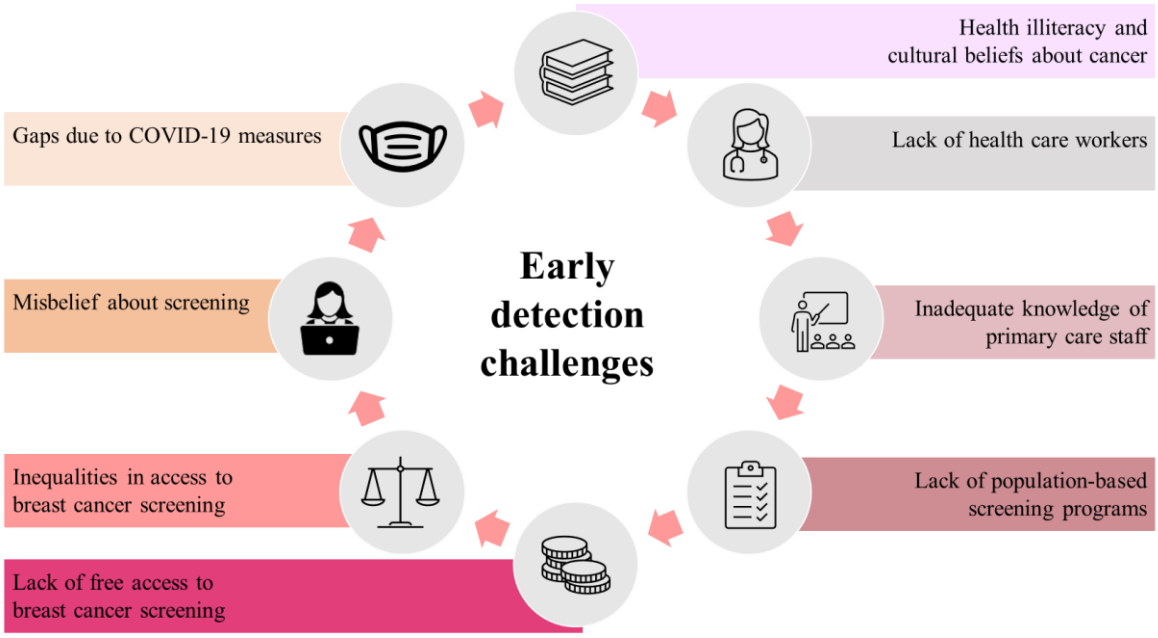

Figure 26: Challenges in early detection of breast cancer in Asia-Pacific.

Challenges relating to self-detection

Health illiteracy and cultural beliefs about cancer

- In Hong Kong, although there is high awareness on breast cancer in general, the awareness and knowledge about TNBC is not as high.[2]
- In South Korea, misconceptions about cancer in the general population might result in a reluctance to visit primary care upon noticing symptoms or to get screened. For instance, in a national survey, 70% of Koreans stated that they thought cancer patients were unable to contribute to society and 60% thought that cancer is nearly impossible to treat (103).
- In Taiwan, a study among women found that 41% believed that doing something morally wrong increased the risk of breast cancer (104).
- In Thailand, there is still a stigma surrounding breast cancer diagnosis in rural areas, often leading to social isolation and discrimination (105).

Lack of health care workers

- In Hong Kong (2.0 physicians per 1,000 inhabitants), South Korea (2.4), Taiwan (2.1), and Thailand (0.8), there is a general shortage of physicians (87). The availability in all markets is below the average in the OECD countries of 3.4 physicians per 1,000 inhabitants (87). In Taiwan, the shortage is partly a result of a cap on medical schools that can only accept a set quota of medical students per year (106).
- In South Korea (7.3 nurses per 1,000 inhabitants) and Thailand (2.8), there is a general shortage of nurses, with availability levels below the OECD average of 8.6 nurses per 1,000 inhabitants (87). Despite health care worker shortages, Koreans have the highest average number of outpatient visits and the highest incidence of hospitalization for treatment (107). This suggests that health care worker scarcity may not be one of the most pressing issues for early breast cancer detection.

Inadequate knowledge of primary care staff

- In Hong Kong, expanding the primary health care system is currently a priority (108). In 2022, a new plan for strengthening the primary care networks in communities was launched (109). This will probably, in the long run, decrease the shortage of primary health care workers and indirectly benefit women who present with breast cancer symptoms. However, current knowledge of nurses practicing in primary care regarding risk factors of breast cancer has been found to be insufficient and most of them did not practice breast examinations regularly (110). More than half of nursing students who had undergone breast self-

[2] Information provided by local experts.

examination classes did not know how to do it or had the erroneous information, according to a survey (111).

- In Australia, a report from the Breast Cancer Network pointed out that women under 40 years reported delays in their diagnosis due to being initially rejected by primary health practitioners when they present with symptoms (112). Some general practitioners are reluctant to continue investigating lumps due to thinking that these women are "too young" for having breast cancer.

Challenges relating to screening

An overview of key features of the breast cancer screening strategies in the included markets as well as participation in the screening programs is provided in Table 5. The main findings are:

- Hong Kong and Thailand lack organized population-based breast cancer screening programs.
- Participation rates vary greatly between markets. South Korea has a comparatively high participation rate. All other markets have a participation rate below the average in the European Union (66%) in 2019 (113).
- The target age group in South Korea is broader and begins earlier than the recommendation by the United States Preventive Services Task Force (50–74 years) and the European Commission (45–74 years) (114, 115).

Table 5: Population-based breast screening programs and results

	Early detection strategy	**Target population**	**Results**
 Australia	-National breast cancer screening program with free mammography screening for women in the target group, every two years (116).	-Women aged 50–74, every two years (116). -Women over the age of 40 and 75 are also eligible for free mammograms, although they are not specifically targeted (116).	-50% of women in the target age group participated in 2019–2020 (117). -49% of all breast cancer cases in women aged 50 to 74 were detected through the program in 2018 (117). -17% of the diagnoses are at stage III and IV (100).
 Hong Kong	-No population-based screening program with mammography (118). -In 2021, a pilot for a breast screening program was launched. It started in three health centers and now is available in all Hong Kong (119). The pilot either lowers mammography fees or fully waives them for low-income groups.	-Women aged 44–69 with a combination of risk factors are recommended to get a mammography every 2 years (119).	-More than 66% of breast cancer patients had never undergone a mammography before diagnosis (47). - The proportion of breast cancer cases diagnosed in stage III and IV was 24% in 2018 (120). - In 2018, only 10% of breast cancer cases were diagnosed in mammograms while being asymptomatic (120).

 South Korea	-National breast cancer screening program with mammography screening every two years (121). - Screening is either free of charge or at a copayment of 10% of the total cost of the procedure depending on a participant's income status (121).	-Women aged 40 and older (121).	-Around 60 to 70% of the target population gets screened (122). -In 2018, 7.2% of cases were diagnosed in stage III and 1% in stage IV (123).
Taiwan	-National breast cancer screening program with mammography screening every two years (124).	-Women aged 45–69 -Women aged 40–44 if they have second-degree relatives with a breast cancer history (124).	-Less than 40% of the target population gets screened (122). -86% of the new breast cancer cases are in early stages (125).
 Thailand	-No nationwide breast screening program. -There are some breast cancer awareness campaigns such as from the Queen Sirikit Centre for Breast Cancer (QSCBC) that mostly focus on teaching self-examination practices (122).	-Women aged 30–70 are recommended to perform breast self-examination (64, 126). -Women aged 40–70 are recommended to get mammography (64, 126).	-Around 70% of women perform breast self-examination regularly (127). -Only 4–6% of women have mammography (128). -41% of breast cancer cases are diagnosed in stage III and IV (122).

Lack of population-based screening programs

- In Hong Kong, there is no formal population-based screening program. NGOs like the HKBCF and Family Planning Association have long advocated for the introduction of an organized population-wide mammography program (120). The Cancer Expert Working Group on Cancer Prevention and Screening (CEWG) did not recommend biannual mammography screening in Hong Kong until 2021 (129). The same year a two-year pilot for a breast screening program was launched (120).

Lack of free access to breast cancer screening

- In Hong Kong, the absence of a screening program means that women need to pay OOP for self-requested mammograms. In a survey, 77% of women in Hong Kong stated that their main barrier for not getting mammograms were the costs of it (130).
- In Thailand, women need to pay OOP for getting mammograms as neither of the three insurance schemes cover mammography screening, explaining partly the very low screening rates (98, 126).

Inequalities in access to breast cancer screening

- In Australia, difficulties in accessing breast cancer screening have been reported for indigenous women, and women living in rural areas and in disadvantaged areas (131). In

2019–2020 the participation rate of indigenous women was 36% while for non-indigenous women it was close to 50% (117).

- In Hong Kong, 75% of women with primary school education have never undergone a mammography screening compared to 50% of women with post-secondary education (47). The same pattern was found for household income; 73% of women in the lowest income group had never undergone a mammography, while the proportion was 40% for women in the highest income group (47). Similar patterns of differences by education and income level were found for breast self-examination rates.
- In Taiwan, women with a high education level and/or income have a higher utilization of mammography screening (132). In addition, women with pre-existent morbidities such as women with dementia, multiple disabilities and intellectual disabilities have lower participation rates in breast cancer screening (133).
- In Thailand, disparities in access to breast cancer screening have been documented across socioeconomic groups. Women who are wealthier, more educated, and live in cities are more likely to get mammograms than women who are lower income, less educated, and live in rural areas (126).

Misbelief about screening

- In Australia, screening rates have remained close to 50%, far from the 70% target, with no significant improvements in recent decades (117, 122, 134). Some of the main reasons why women do not get screened are (i) denial and the attitude “that it is not going to happen to me”, (ii) fear associated with dying, cancer and a long term illness, (iii) the discomfort of the mammogram, (iv) self-consciousness and embarrassment, (v) accessibility (in some locations), (vi) lack of time, (vii) radiation concerns from the x-ray, (viii) concerns about the accuracy of mammograms, (ix) language barriers, and (x) procrastination (135).
- In South Korea, according to a recent survey, half of women aged 20–59 who did not get screened did so because they did not feel the need to (49%), followed by screening not being recommended by a clinical institution (37%), fear of getting screened (30%), costs of getting a screening (22%), and embarrassment (15%) (136). An older study also found that women did not attend screening because of a lack of prioritization and being afraid of a breast cancer diagnosis (137).
- In Taiwan, the National Health Survey of 2017 indicated that women who did not get screened did so because they did not perceive the need to (47.9%), were too busy (26.0%), or were afraid of a painful examination process (14.4%) (138). Similar barriers to attend breast cancer screening were also identified in an older survey from 2012 (104).

Gaps due to COVID-19 measures

Delays in breast cancer screening as a result of disruptions in the provision of health care during the pandemic will likely increase the number of cases diagnosed in late stages in the coming years.

- In Australia, as shown in Table 5, the participation rate was 50% for women aged 50 to 79 for the period 2019–2020 vs. 55% in the period of 2017–2018 in the national breast screening program (99, 117).
- In Taiwan, despite the fact that the COVID-19 incidence was lower than in other countries of the region, studies have suggested that the pandemic affected early breast cancer detection. The number of early-stage breast cancer cases and total breast cancer cases decreased by 38% and 10%, respectively, from 2019 to 2020 (139).
- In South Korea, the participation rate in breast cancer screening declined from 70% in 2019 to 63% in 2020 (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 (141). 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 (84, 85, 142).

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 (143). Breast cancer patients with a long delay of ≥61 days between diagnosis and start of neoadjuvant systemic therapy have a 28% increased risk of subsequent mortality compared to patients with a short delay of 0–30 days (144).

Figure 27 summarizes key challenges associated with the diagnostic process of TNBC in the included Asia-Pacific markets. Note that not all challenges apply to every market.

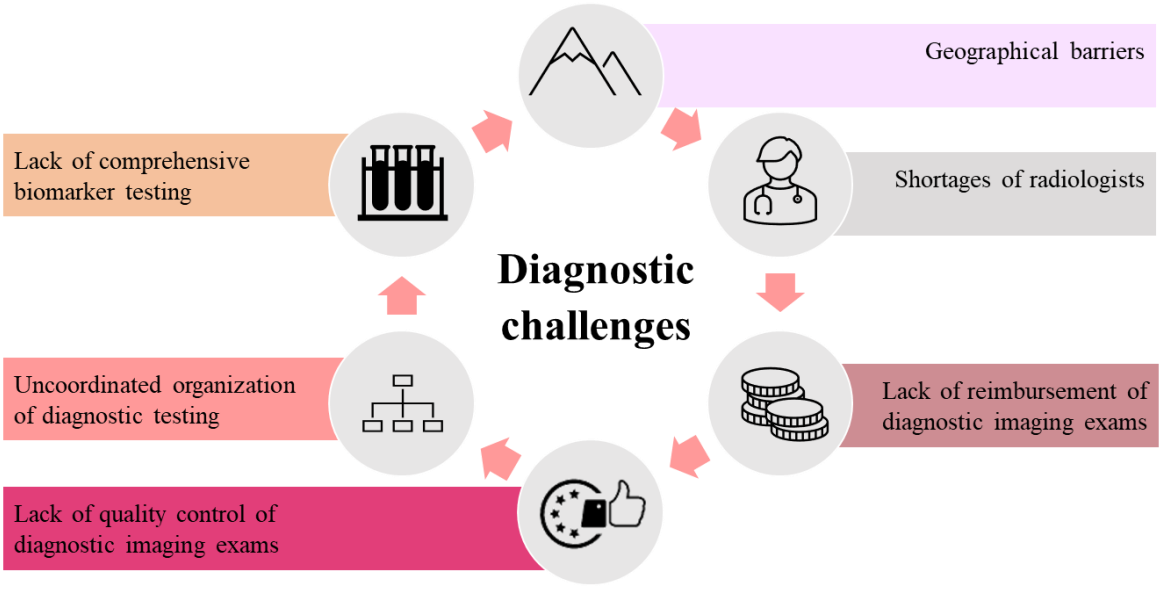

Figure 27: Challenges in the diagnostic process of TNBC in Asia-Pacific.

Geographical barriers

- In Australia, rules for receiving Medicare rebates for diagnostic imaging services encourage multiple visits, which is disadvantageous for patients living in remote areas. Patients cannot receive a free biopsy after an ultrasound on the same day due to the multiple service rule according to the Breast Cancer Network Australia (145). This compels patients living in remote areas to choose between paying OOP for multiple services on the same day or delaying diagnosis.
- The Bangkok Metropolitan Region is home to 25% of Thailand's breast diagnostic devices, including mammography machines and MRI scanners. In other provinces, diagnostic equipment is less accessible and women face the burden of spending time on and paying for transportation which acts as a deterrent for accessing diagnostic services and uptake of treatment (98).

Shortages of radiologists

- In Australia, the shortage of physicians specialized in diagnostic radiology was one of the eight highest shortages among medical specialties in 2022 (146). It is estimated that by 2030, the undersupply of radiologists and radiation oncologists will be 25% and 63%, respectively, lower than the estimated number that is needed to cover the demand (145).
- In Thailand, there is a lack of radiologists to perform mammograms (126).

Lack of reimbursement of diagnostic imaging exams

- In Australia, breast MRI scans are not covered by the Medicare Benefits Schedule (MBS), necessitating patients to pay OOP for this examination (145). MRI scans along with genetic

tests have been found to be some of the greatest components of OOP of breast cancer patients in Australia (79).

Lack of quality control of diagnostic imaging exams

- In South Korea, there has been a surge in the number of breast diagnostic imaging tests in the past. Between 2013 and 2016, the number of breast MRI scans more than doubled and breast ultrasound increased more than ten times (147). It is unlikely that this has been driven by an increase in the underlying medical demand. Medical auditing to ensure quality control has not been prioritized in the past. In a survey of 312 breast radiologists, more than 60% stated that they did not perform regularly medical audits (147).

Uncoordinated organization of diagnostic testing

- In Thailand, tests for hormone receptor/HER2 status may not be tested in parallel with staging but rather sequentially. This leads to delays in the diagnostic process.[3]

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, tests for BRCA1/2 mutations and PD-L1 status are not yet widely implemented except in South Korea.

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

	Tests for hormone receptor and HER2 status	**Tests for BRCA1/2 (with therapeutic intent)**	**Tests for PD-L1**
 Australia	-Hormone receptor/HER2 status is routinely tested (148).	-Tests are not reimbursed in the public sector (MBS). -There is currently a submission for reimbursing BRCA1/2 mutation tests for patients with HER2-negative high-risk early-stage breast cancer (149).	-Tests are not reimbursed in the public sector (MBS). -Patient programs by pharmaceutical companies pay for testing in some instances.
 Hong Kong	-Hormone receptor/HER2 status is routinely tested.	-Tests are not reimbursed in the public sector. -Patient programs by pharmaceutical companies pay for testing.	-Tests are not reimbursed in the public sector.
 South Korea	-Hormone receptor/HER2 status is routinely tested (150).	- Tests are reimbursed by the NHI.	-Tests are reimbursed by the NHI.
Taiwan	-Hormone receptor/HER2 status is routinely tested (150).	-Tests are not reimbursed in the public sector.	-Tests are not reimbursed in the public sector.

[3] Information provided by local experts.

Thailand	-Hormone receptor/HER2 status is routinely tested and reimbursed.	-Tests are not reimbursed in the CSMBS/SSS/UCS.	-Tests are reimbursed in the CSMBS. -Tests are not reimbursed in the SSS and UCS.

Notes: Unless sources are provided in the table, information was sourced from local experts. PBS = Medicare Benefits Schedule, NHI = National Health Insurance.

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) (141).

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 (151). 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 (85).

Figure 28 summarizes key challenges associated with the treatment of TNBC in the included Asia-Pacific markets. Note that not all challenges apply to every market.

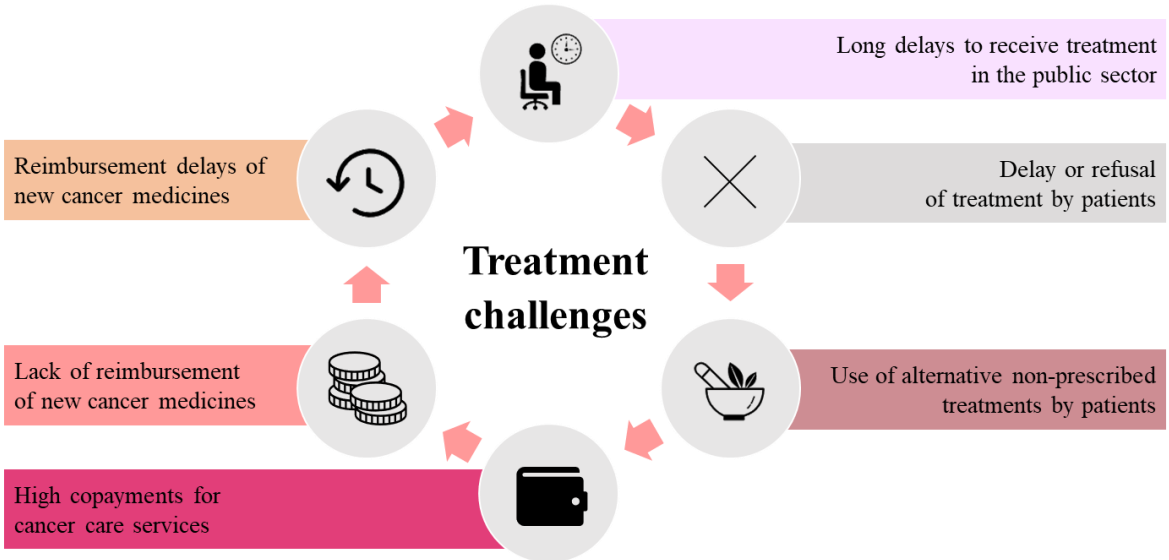

Figure 28: Challenges in the treatment of TNBC in Asia-Pacific.

Long delays to receive treatment in the public sector

- In Hong Kong, the median time from consulting a physician at a hospital to treatment initiation is 11 days in private hospitals compared to 49 days in public hospitals (122). This is partly caused by a lack of health care staff in public hospitals (122).

Delay or refusal of treatment by patients

- In Taiwan, older breast cancer patients have an increased tendency to delay or refuse treatments (152). Major factors of refusing treatment were fear of surgery, poor response to therapy and poor quality of life following therapy, fear of adverse effects of chemotherapy or radiation therapy, economic burden of household or busy job, and feeling guilty (152). Patients who delay or refuse therapy have lower 5-year overall survival rate compared with the treated patients (152).

Use of alternative non-prescribed treatments by patients

- Women in Thailand are at an increased risk of delaying treatment due to trying alternative medicines first (122). The use of alternative non-prescribed medicines also during treatment with cancer medicines is common, with up to three fourths of breast or gynecological cancer patients using them (153). This puts women at a risk of adverse drug interactions (153).

High copayments for cancer care services

Patient access to cancer medicines and other medical services that are reimbursed by the public payer might be limited by copayments. In the absence of full price coverage, patients incur OOP for the copayment. If there is no cap on the total amount of OOP, access to treatment will be restricted, especially for economically disadvantaged groups. Patient copayments for cancer medicines are common in the Asia-Pacific markets; see Table 7.

- A systematic review of Australian cancer patients found that OOP for medical services (including cancer medicines) puts a significant strain on cancer patients and their families. The financial burden and psychological distress were associated with nonadherence to cancer-specific treatment which included delaying, modifying, forgoing or not completing recommended treatment (154).
- In Thailand, around 24% of all cancer patients and their families face financial catastrophe (defined as OOP payments for medical services and non-medical services exceeding 30% of the annual household income) (155).

Table 7: Policies for copayments of cancer medicines

Australia	Maximum copayment of AU$30 per prescription of medicines in the Pharmaceutical Benefits Scheme (PBS) as of 2023.
Hong Kong	• Full coverage of medicines which are listed as special drugs and general drugs. • Copayment for medicines which are reimbursed through the Community Care Fund / Samaritan Fund according to patients' asset level. • Self-pay for medicines which are only listed as self-financed item in the Hospital Authority Drug Formulary.
South Korea	Copayments for cancer medicines listed in the national formulary of up to 5%. Copayments for 'Selective Reimbursement' medicines that are exceptionally applicable to some cancer medicines with uncertain cost-effectiveness and clinical benefit are 30% or 50%.
Taiwan	Copayments for outpatient prescription cancer medicines listed in the national formulary of 20% but capped at TW$300 (around USD 10).

Thailand	• Beneficiaries in the UCS and SSS have full coverage of listed medicines. • Beneficiaries in the CSMBS can either have full coverage or add-on payments on a fee-for-service for listed cancer medicines.

Source: (156-159) and information provided by local experts.

Lack of reimbursement of new cancer medicines

A defining challenge for cancer patients in the region is access to new cancer medicines. Figure 29 shows that the five Asia-Pacific markets grant regulatory approval to innovative cancer medicine-indications to a high degree, with 82–100% of all indications with US FDA also being approved locally (160). However, only on average 48% of these indications were reimbursed in these markets, ranging from 5% in Thailand to 63% in South Korea and Taiwan (160). The latter markets trail the regional leader Japan, which reimbursed 89% of indications.

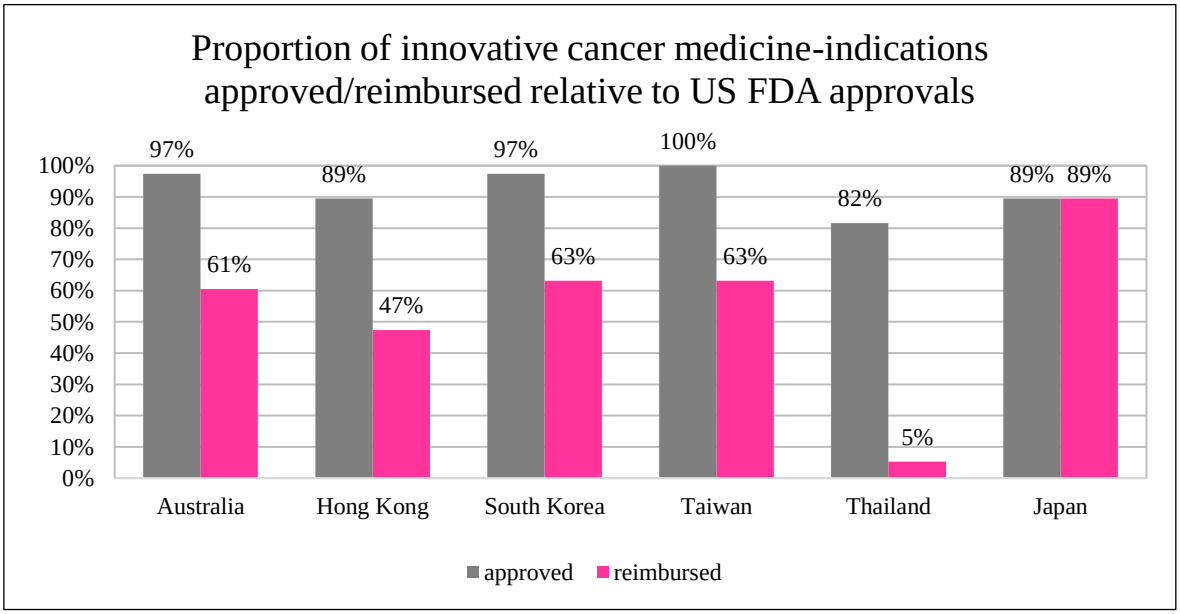

Figure 29: Proportion of innovative cancer medicine-indications approved/reimbursed relative to US FDA approvals.

Notes: Numbers reflect the status on Sep 30, 2020. 100% represents 38 medicine-indications across five solid tumor types approved by the US FDA on Sep 30, 2020 which had a high ESMO-MCBS score. Source: (160).

Reimbursement delays of new cancer medicines

- Cancer medicines face considerable delays between regulatory approval and reimbursement. A recent analysis of innovative cancer medicine-indications with US FDA approval between 2010 to 2020 showed that the local median delay between regulatory approval and reimbursement ranged from around 1.5 years in Australia and South Korea to around 2 years in Hong Kong and Taiwan (160). In Thailand, the median delay might be longer than 10 years (160).
- In Australia, cancer medicines have the longest average timelines to get listed in the national formulary (496 days) compared with medicines in other disease (e.g., 149 days for mental health, 442 days for cardiovascular diseases) (161).

- In South Korea, one of the causes for delays is the lengthy reimbursement procedure and the various committees engaged in assessment process. New cancer medicines must go through the Oncology Drug Assessment Committee at the Health Insurance Review and Assessment Service (HIRA) to evaluate clinical usefulness and reimbursement guidelines, the Drug Review Evaluation Committee at the HIRA to assess cost-effectiveness, the NHIS (National Health Insurance Service) to negotiate prices, and finally the NHI Policy Deliberation Committee at the Ministry of Health and Welfare as the final decision-making committee.[4]

[4] Insights provided by external experts.

4. Societal impact of improved TNBC care

The previous chapter pointed to many opportunities to improve the care of TNBC patients in Asia-Pacific. The quality of care provided to patients determines not just their health outcomes, but also has wider implications for society. Figure 30 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.

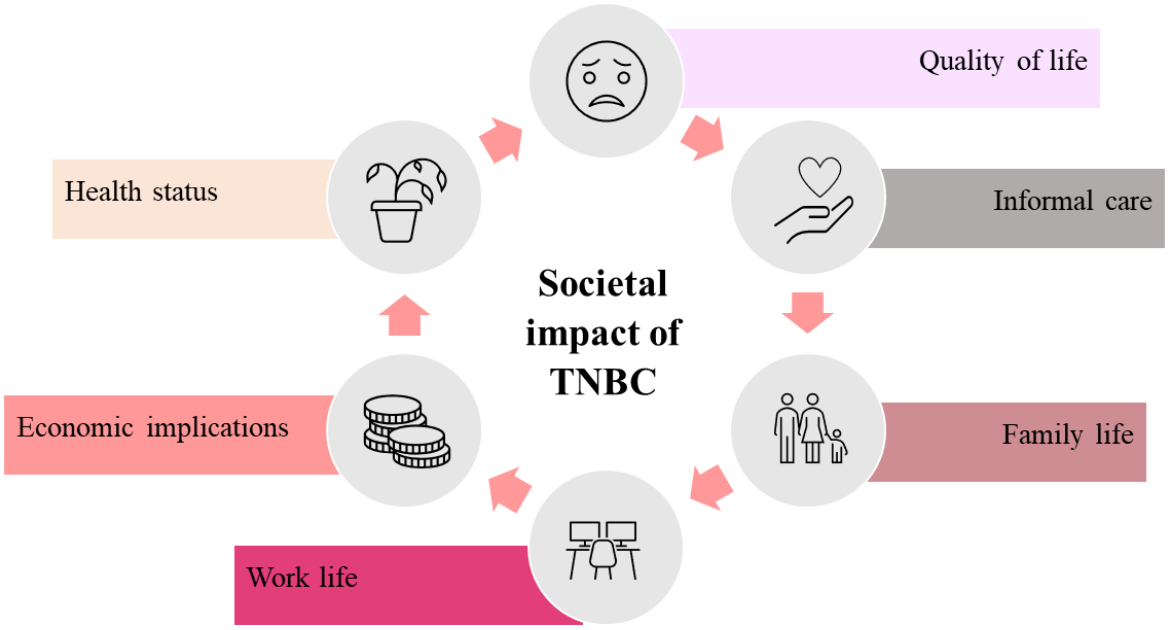

Figure 30: Elements of the societal impact of TNBC.

Example: Improving early detection

Population-based mammography screening programs are not operating effectively in many markets of the Asia-Pacific region. For this reason, in some of the markets, comparatively many women with breast cancer are still diagnosed at advanced stages. 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 markets 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 close to 95% in stage I but only 11% in stage IV in Taiwan (69); see section 2.2).

- **Family life and informal care**: The lower symptom burden of breast cancer in early stages than in late stages may reduce the amount of informal care required by patients. This may also positively affect family life. A diagnosis at an earlier stage may also lower the psychological burden on family members due to a reduced likelihood of losing a mother/spouse/partner.
- **Work life**: More women could continue to work during their initial treatment or resume work after it, because of the lower symptom burden of breast cancer in early stages than in late stages.
- **Economic implications**: The treatment costs might decrease, because the costs of treating TNBC are lower at early stages than at late stages. Indeed, the medical costs for stage IV TNBC are three to five times as high as for stage I TNBC in Western high-income countries (81), and there is evidence of a similar cost pattern in the Asia-Pacific region (78); 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 Asia-Pacific 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 Asia-Pacific. These recommendations can be grouped into three main areas as shown in Figure 31. 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.

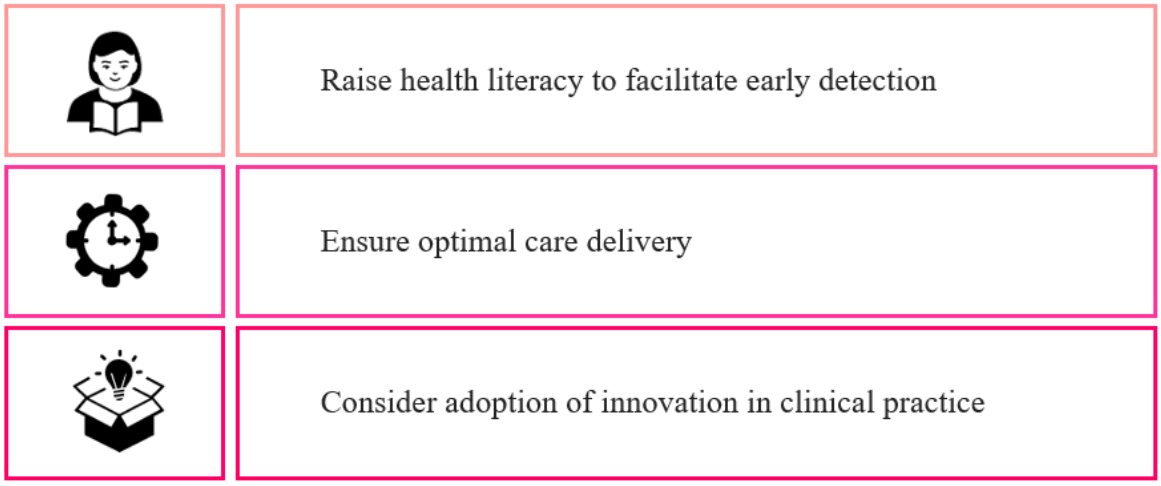

Figure 31: Main areas of improvement for TNBC care.

Area 1: Raise health literacy to facilitate early detection

Improve breast cancer prevention

More than 20% of breast cancer cases in various locations in the Asia-Pacific region are potentially preventable, because they are caused by modifiable risk factors, including obesity/overweight and physical inactivity. The promotion of a healthy diet and lifestyle is therefore important to avert 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, in particular in locations such as Thailand with no national breast cancer screening program or in locations where participation in existing screening programs is low. The promotion of health literacy and regular self-examination needs to be prioritized. In various Asia-Pacific markets, NGOs play an essential role in offering educational campaigns. To maximize the impact of these private campaigns, they could be combined with government-led public health campaigns.

Enhance involvement of primary care in early detection

Primary care can play a crucial role in improving outcomes for breast cancer patients. The recruitment of primary health care workers should be prioritized, and they need to be trained in early breast cancer detection. They should also encourage regular 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, ovarian, or pancreatic cancer) can potentially increase the chances of early diagnosis.

Promote participation in screening programs

Apart from South Korea, all markets have comparatively low participation rates in breast cancer screening programs. Addressing misbeliefs about screening by raising women's knowledge of the potential benefits and harms of participating in organized screening programs is critical for enhancing early detection.

Tailor screening promotion campaigns to women in vulnerable groups

Screening and self-breast clinical examination rates are substantially lower among minorities and vulnerable groups throughout the Asia-Pacific markets. Screening programs must prioritize reaching out to these groups by enhancing geographical access to mammography and lowering cost barriers to ensure that the programs are accessible to everybody.

Area 2: Ensure optimal care delivery

Invest in recruitment and retention of primary care workers

Primary care can play a crucial role in improving outcomes for breast cancer patients. Most Asia-Pacific markets suffer from significant shortages of primary care physicians and nurses. Health systems are overwhelmed by the rising demand for health care services, which restricts the services that the public sector can deliver, particularly in rural areas. Attracting and improving the system's capacity to retain primary health care workers should be prioritized through multifaceted measures that include financial and non-financial incentives.

Implement breast cancer screening programs and guarantee free access

Hong Kong and Thailand lack national organized population-based screening programs. The introduction of screening programs, possibly modelled on successful examples in the region such as in South Korea, needs to be a priority. A first step towards a population-based screening program could be a risk-stratified program that targets only a subgroup of women at an increased risk of breast cancer.

Broaden the target age group in screening programs

Markets in the region that already have established screening programs could consider broadening the target group to women aged 45–74 years in line with the latest recommendation from the Council of the European Union.

Establish clear care pathways

Long delays between diagnosis and start of treatment, especially in the public sector, may occur in some markets in Asia-Pacific. These delays decrease the chances of positive treatment outcomes. 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 and the sequence of diagnostic tests to be made before treatment start.

Assure high quality of breast cancer imaging

Even though mammography is the main imaging method during the diagnostic process, alternative imaging methods (ultrasound and MRI) may also be medically necessary in some women. Access to these alternative methods should be ensured, e.g., for women with high breast density or known BRCA1/2 mutations. At the same time, these methods should not be overused, and regular medical auditing should be performed to ensure quality control.

Recruit and train radiologists for breast imaging

Breast cancer diagnosis relies heavily on mammography imaging. Shortages of radiologists cause delays in getting a breast cancer diagnosis. This situation is expected to deteriorate along with the growing numbers of women who require mammography in the coming years. To avoid bottlenecks in the diagnostic process, current staff shortages of radiologists need to be addressed.

Support patient adherence to treatment

Caps on patient copayments for reimbursed cancer care services should be introduced in countries where they do not yet exist. The caps should be of a size that prevents nonadherence to treatment because of financial reasons, especially among economically disadvantaged patients.

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. These diagnostic tests need to be incorporated in local clinical guidelines and reimbursed by public payers to guarantee broad access to patients. Currently, only some of these tests are covered in the public sector in some of the Asia-Pacific markets under study. They may be available through special patient access programs run by pharmaceutical companies or paid for out-of-pocket by patients.

Update local clinical guidelines

New treatment options in TNBC that have become available since 2018 are already incorporated in international clinical guidelines. However, local guidelines in Asia-Pacific countries need to be updated as well when new diagnostic tests and treatments become available in the local setting. This would help to choose the appropriate treatment in the increasingly complex treatment landscape for TNBC.

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 and/or adjuvant therapy. Clinical staff needs to be trained to ensure optimal use of novel treatment options.

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Annex – Summary cards

Australia

Population: 25.7 million (2021)
GDP per capita: USD 59,934 (2021)
Life expectancy: 83.2 years (2020)
Total health expenditure: 9.9% of GDP (2019)
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 14% 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
• Health spending on cancer care accounted for around 4.5% of the total health expenditure in 2013, which is less than what many countries in Europe (around 6% in 2018) spend on cancer care and also less than other high-income markets like Japan (7.5% in 2018). • According to the WHO, at most 30% of all breast cancer cases are theoretically preventable as they are caused by modifiable risk factors. The main modifiable risk factors are obesity/overweight and physical inactivity. In Australia, an increasing proportion of adult women is obese (nearly 30% in 2016), and more than 30% of women are not sufficiently physically active, which increases the risk of getting breast cancer.	• Consider increasing public funding on cancer care. • Create effective national prevention strategies to halt rising levels of obesity and physical inactivity.

Early detection

Challenges	Recommendations
• The national breast cancer screening program for women aged 50–74 achieves a participation rate of around 50%, which is below the national target of 70% and the average participation rate in the European Union of 66%. Patient preferences and behavior partly hamper participation. The main reasons why women do not get screened are related to (i) denial and the attitude "that it is not going to happen to me", (ii) fear of cancer diagnosis, (iii) the discomfort of the mammogram, (iv) self-consciousness and embarrassment, (v) accessibility (in some locations). • There are significant disparities in breast cancer screening participation rates across socioeconomic groups, with lower rates among indigenous women and women living in rural areas. • Due to COVID-19 control measures, disruptions in the breast cancer screening program and changes in patient behavior have led to reductions in screening.	• Raise awareness about the benefits of breast cancer screening. • Run campaigns to increase participation of vulnerable groups in the breast cancer screening program. • Intensify efforts to boost participation in breast cancer screening in the aftermath of the COVID-19 pandemic.

Diagnostic services

Challenges	Recommendations
• Medicare rebate rules for diagnostic imaging services encourage multiple visits, which is problematic for patients living in remote areas who must choose between paying out-of-pocket for multiple services on the same day or delaying their diagnosis. • Shortages of diagnostic radiology specialists, as well as an expected undersupply of radiation oncologists, may jeopardize the timely availability of essential diagnostic services. • MRI scans are not covered by the Medicare Benefits Schedule and are an important component of out-of-pocket from breast cancer patients. • Comprehensive biomarker testing for BRCA and PD-L1 status were not covered in the public sector at the end of 2022. Either patients need to pay for the tests out-of-pocket or pharmaceutical companies cover them through patient support programs.	• Review coverage rules for receiving multiple diagnostic imaging services at a single health care visit. • Invest in recruitment and skills of health care professionals in radiology. • Consider covering medically necessary MRI scans. • Expand access to biomarker testing for BRCA and PD-L1 status.

Access to treatment

Challenges	Recommendations
• There is limited patient access to innovative cancer medicines. Only 61% of US FDA-approved innovative cancer medicine-indications were reimbursed locally in 2020, compared to 63% in South Korea and Taiwan and 89% in Japan. • Cancer medicines face considerable delays between regulatory approval and reimbursement. A recent analysis of innovative cancer medicine-indications with US FDA approval between 2010 to 2020 showed that the local median delay between regulatory approval and reimbursement was around 1.5 years compared to 1–3 months in Japan. Another analysis showed that cancer medicines face longer reimbursement timelines until getting listed in the national formulary compared medicines in other disease areas. • Out-of-pocket payments for medical services (including cancer medicines) put a significant – financial and psychological – strain on cancer patients and their families, which may lead to nonadherence to cancer-specific treatment.	• Enhance patient access to cancer medicines in the public sector. • Accelerate timelines for the inclusion of cancer medicines with high clinical benefit in the national formulary. • Review current limits for maximum co-payments for medical services to reduce unsustainable out-of-pocket payments (such as done via the reduction of the prescription fee in the PBS from AU$42.50 to AU$30 in 2023).

Hong Kong

Population: 7.4 million (2021)
GDP per capita: USD 49,660 (2021)
Life expectancy: 85.3 years (2020)
Total health expenditure: 6.2% of GDP (2019)
Source: World Bank and Department of Health for Hong Kong.

Triple-Negative Breast Cancer (TNBC)

- Breast cancer is the most common cancer type in women (29% of all new cancer cases) and responsible for 12% of all female cancer deaths.
- Around 10% 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
• Public spending on health accounts for 3% of GDP, which is less than other high-income markets in the region such as Australia, South Korea, and Taiwan, which spend 7%, 5%, and 4%, respectively. The absolute total health expenditure per capita at USD 3,000 is also lower than in Australia (around USD 5,400). • According to the WHO, at most 30% of all breast cancer cases are theoretically preventable as they are caused by modifiable risk factors. The main modifiable risk factors are obesity/overweight and physical inactivity. In Hong Kong, an increasing proportion of adult women is obese (more than 10% in 2016), and 18% of women are not sufficiently physically active, which increases the risk of getting breast cancer.	• Increase public spending on health care to bring Hong Kong closer to the leading high-income markets in the region. • Create effective national prevention strategies to halt rising levels of obesity and physical inactivity.

Early detection

Challenges	Recommendations
• Although there is high awareness on breast cancer in general, the awareness and knowledge about TNBC is not as high. • There is a lack of early detection training for breast cancer nurses working in primary health care. This can lead to delays in the early diagnosis of women with breast cancer symptoms. • There are significant disparities in breast self-examination rates and getting mammograms according to the level of educational attainment and household income of women. • There is no organized population-based breast screening program. Women aged 44–69 are only recommended to get screened, but the responsibility falls on them. This leads to low screening rates. In 2018, only 10% of breast cancer cases were diagnosed in mammograms while being asymptomatic. In 2021, a pilot for breast cancer screening was launched, but it is unclear if it will become permanent. • The absence of a screening program leads to out-of-pocket expenditure for self-requested mammograms. A high proportion of women state that this is one of the main barriers to getting screened.	• Raise awareness of breast cancer/TNBC symptoms among women. • Improve the training of breast cancer nurses in primary health care. • Run campaigns to increase self-examination among vulnerable groups. • Turn the current pilot for breast cancer screening into a permanent organized population-based program with free mammograms.

Diagnostic services

Challenges	Recommendations
• Comprehensive biomarker testing for BRCA and PD-L1 status were not covered in the public sector at the end of 2022. Either patients need to pay for the tests out-of-pocket or pharmaceutical companies cover them through patient support programs.	• Expand access to biomarker testing for BRCA and PD-L1 status.

Access to treatment

Challenges	Recommendations
• A lack of health care staff in public hospitals causes delays in the time from consulting a physician at a hospital to treatment initiation. • There is limited patient access to innovative cancer medicines. Only 47% of US FDA-approved innovative cancer medicine-indications were reimbursed locally in 2020, compared to around 61–63% in Australia, South Korea, and Taiwan and 89% in Japan. • Cancer medicines face considerable delays between regulatory approval and reimbursement. A recent analysis of innovative cancer medicine-indications with US FDA approval between 2010 to 2020 showed that the local median delay between regulatory approval and reimbursement was around 2 years compared to 1–3 months in Japan and 1.5 years in Australia and South Korea.	• Ensure adequate staffing in public hospitals to avoid unnecessary treatment delays. • Enhance patient access to cancer medicines in the public sector. • Accelerate timelines for the inclusion of cancer medicines with high clinical benefit in the national formulary.

South Korea

Population: 51.7 million (2021)
GDP per capita: USD 34,757 (2021)
Life expectancy: 83.4 years (2020)
Total health expenditure: 8.2% of GDP (2019)
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 8% of all female cancer deaths.
- Around 11% 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
• Public spending on health accounts for 5% of GDP, which is less than other high-income markets in the region, such as Australia which spends 7%. The absolute total health expenditure per capita at USD 2,600 is also lower than in Australia (around USD 5,400) and Hong Kong (around USD 3,000). • According to the WHO, at most 30% of all breast cancer cases are theoretically preventable as they are caused by modifiable risk factors. The main modifiable risk factors are obesity/overweight and physical inactivity. In South Korea, an increasing proportion of adult women is obese (5% in 2016), and more than 40% of women are not sufficiently physically active, which increases the risk of getting breast cancer.	• Increase public spending on health care to bring South Korea closer to high-income markets in the region. • Create effective national prevention strategies to halt rising levels of obesity and physical inactivity.

Early detection

Challenges	Recommendations
• Early detection of breast cancer might be partly hampered by misconceptions about cancer in the general population. A majority of Koreans think cancer is nearly untreatable and that patients cannot contribute to society. • Participation in the national breast cancer screening program is comparatively high at around 60–70%. The majority of women who do not get screened report that this is because they do not feel the need/urgency to, fear of getting screened, the costs of getting screened, and embarrassment. • Due to COVID-19 control measures, disruptions in the breast cancer screening program and changes in patient behavior have led to reductions in screening.	• Raise awareness about breast cancer, including early symptoms and survival chances, among women. • Run awareness campaigns to increase participation in the breast cancer screening program. • Intensify efforts to boost participation in breast cancer screening in the aftermath of the COVID-19 pandemic.

Diagnostic services

Challenges	Recommendations
• Medical auditing of breast diagnostic imaging (in particular MRI scans and ultrasounds) to ensure quality control has not been prioritized in the past. Many radiologists state not performing regular medical audits. • BRCA and PD-L1 tests needed prior to the administration of newer TNBC medicines have been reimbursed by the NHI in 2022. The implementation in clinical practice across all cancer clinics is still pending.	• Prioritize quality assurance of breast diagnostic imaging. • Ensure implementation of tests for BRCA mutations and PD-L1 status in clinical practice for all eligible patients.

Access to treatment

Challenges	Recommendations
• There is limited patient access to innovative cancer medicines. Only 63% of US FDA-approved innovative cancer medicine-indications were reimbursed locally in 2020, similar to the situation in Australia and Taiwan, but below the 89% in Japan. • Cancer medicines face considerable delays between regulatory approval and reimbursement. A recent analysis of innovative cancer medicine-indications with US FDA approval between 2010 to 2020 showed that the local median delay between regulatory approval and reimbursement was around 1.5 years compared to 1–3 months in Japan. One of the causes for delays is the lengthy reimbursement procedure and the various committees engaged in assessment process. • Co-payments for cancer medicines listed in the national formulary of generally up to 5% present a significant burden for cancer patients and their families with limited private financial means.	• Enhance patient access to cancer medicines in the public sector. • Accelerate timelines for the inclusion of cancer medicines with high clinical benefit in the national formulary. • Review current limits for maximum co-payments for cancer medicines to reduce unsustainable out-of-pocket payments.

Taiwan

Population: 23.2 million (2022)
GDP per capita: USD 32,914 (2022)
Life expectancy: 80.9 years (2021)
Total health expenditure: 6.1% of GDP (2019)
Source: National Statistics Republic of China (Taiwan)

Triple-Negative Breast Cancer (TNBC)

- Breast cancer is the most common cancer type in women (26% of all new cancer cases) and responsible for 13% of all female cancer deaths.
- Around 9% 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
• Public spending on health accounts for 4% of GDP, which is less than other high-income markets in the region such as Australia and South Korea, which spend 7% and 5%, respectively. The absolute total health expenditure per capita at USD 1,600 is also lower than in Australia (around USD 5,400), Hong Kong (USD 3,000), and South Korea (USD 2,600). • According to the WHO, at most 30% of all breast cancer cases are theoretically preventable as they are caused by modifiable risk factors. The main modifiable risk factors are obesity/overweight and physical inactivity. In Taiwan, an increasing proportion of adult women is obese (9% in 2016), which increases the risk of getting breast cancer.	• Increase public spending on health care to bring Taiwan closer to high-income markets in the region. • Create effective national prevention strategies to halt rising levels of obesity and physical inactivity.

Early detection

Challenges	Recommendations
• Early detection of breast cancer might be partly hampered by misconceptions about breast cancer in the general population. In addition, there is widespread superstition among women that immoral behavioral can lead to breast cancer. • The population-based breast cancer screening program for women aged 45–69 only achieves a participation rate of less than 40%. Women who decide to not take part in the screening program do so because they did not perceive the need to, were too busy, or were afraid of a painful examination process. • There are significant disparities in breast cancer screening participation rates between women from different socioeconomic groups and between women with and without pre-existent morbidities. • Due to COVID-19 control measures, disruptions in the breast cancer screening program and changes in patient behavior have led to reductions in screening.	• Raise awareness about breast cancer, including risk factors and early symptoms, among women. • Run awareness campaigns to increase participation in the breast cancer screening program, with a particular focus on raising participation in vulnerable groups. • Intensify efforts to boost participation in breast cancer screening in the aftermath of the COVID-19 pandemic.

Diagnostic services

Challenges	Recommendations
• Comprehensive biomarker testing for BRCA and PD-L1 status were not covered in the public sector at the end of 2022. Patients currently need to pay for the tests out-of-pocket. This limits patient access to the already reimbursed BRCA-targeted medicines.	• Expand access to biomarker testing for BRCA and PD-L1 status.

Access to treatment

Challenges	Recommendations
• Older breast cancer patients have an increased tendency to delay or refuse treatments, leading to worse health outcomes. Major factors of refusing treatment were fear of surgery, poor response to therapy and poor quality of life following therapy, fear of adverse effects of chemotherapy or radiation therapy, economic burden of household or busy job, and feeling guilty. • There is limited patient access to innovative cancer medicines. Only 63% of US FDA-approved innovative cancer medicine-indications were reimbursed locally in 2020, similar to the situation in Australia and South Korea, but below the 89% in Japan. • Cancer medicines face considerable delays between regulatory approval and reimbursement. A recent analysis of innovative cancer medicine-indications with US FDA approval between 2010 to 2020 showed that the local median delay between regulatory approval and reimbursement was around 2 years compared to 1–3 months in Japan and 1.5 years in Australia and South Korea.	• Improve the physician-patient communication on benefits and risks of therapy options, while accepting patient choice. • Enhance patient access to cancer medicines in the public sector. • Accelerate timelines for the inclusion of cancer medicines with high clinical benefit in the national formulary.

Thailand

Population: 69.9 million (2021)
GDP per capita: USD 7,233 (2021)
Life expectancy: 77.3 years (2020)
Total health expenditure: 3.8% of GDP (2019)
Source: World Bank

Triple-Negative Breast Cancer (TNBC)

- Breast cancer is the most common cancer type in women (23% of all new cancer cases) and responsible for 15% 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
• The three public health insurance schemes (UCS, SSS, CSMBS) cover the entire population. Yet there are profound inequalities in the range of health services available along the entire patient journey by each scheme, especially in the CSMBS compared to the UCS and SSS. • Public spending on health accounts for 3% of GDP, which is less than the informal WHO target of 5%. The absolute public health expenditure per capita at around USD 210 is only a fraction of what high-income markets in the region spend (Hong Kong and South Korea both around USD 1,550 and Taiwan USD 1,000). • Health spending on cancer care accounted for around 2% of the total health expenditure in 2018, which is less than what many countries in Europe (around 6% in 2018), Australia (4.5% in 2013), and Japan (7.5% in 2018) spend on cancer care. • According to the WHO, at most 30% of all breast cancer cases are theoretically preventable as they are caused by modifiable risk factors. The main modifiable risk factors are obesity/overweight and physical inactivity. In Thailand, an increasing proportion of adult women is obese (13% in 2016), and more than 28% of women are not sufficiently physically active, which increases the risk of getting breast cancer. There is very little knowledge among women about the link of these lifestyle factors to breast cancer.	• Strive for a more equitable provision of health care services in all three public health insurance schemes. • Increase public spending on health care to bring Thailand closer to high-income markets in the region. • Increase public funding of cancer care. • Create effective national prevention strategies to halt rising levels of obesity and physical inactivity, and spread awareness about these risk factors.

Early detection

Challenges	Recommendations
• A general shortage of health care workers can contribute to long waiting times to access health care services in some areas. This can lead to delays in the early diagnosis of women with breast cancer symptoms. • Early detection of breast cancer might be hampered by misconceptions and stigma surrounding breast cancer in the general population. A breast cancer diagnosis might lead to social isolation and discrimination. • There is no single nationwide organized population-based breast screening program. Women aged 40–70 are only recommended to get a mammography, but the responsibility falls on them. This leads to very low mammography screening rates of only 4–6%. Low participation partly explains why a high proportion of breast cancer diagnoses are made at an advanced clinical stage. • The absence of a screening program leads to out-of-pocket costs for self-requested mammograms. • There are disparities in the use of breast cancer screening across socioeconomic groups. Women who are wealthier, more educated, and live in cities are more likely to get mammograms than women from the least privileged groups.	• Invest in recruitment and training of health care workers. • Raise awareness about breast cancer, including risk factors and early symptoms, among women. • Implement a national organized population-based breast cancer screening program with free mammograms. • Run campaigns to increase participation breast cancer screening in vulnerable groups.

Diagnostic services

Challenges	Recommendations
• Geographic access to breast diagnostic devices (mammography machines and MRI scanners) is limited in provinces outside the Bangkok Metropolitan Region. This creates a burden for women to spend time and money on transportation, which acts as a deterrent for accessing diagnostic services and uptake of treatment. • There is a shortage of radiologists performing mammograms, which can lead to long waiting times and delays in the early diagnosis of women with breast cancer symptoms. • Tests for hormone receptor/HER2 status may not be tested in parallel with staging but rather sequentially. This leads to delays in the diagnostic process. • Comprehensive biomarker testing for BRCA status and PD-L1 status (only in SSS and UCS) were not covered in any public health insurance scheme at the end of 2022.	• Improve geographic access to essential diagnostic services in all provinces. • Invest in recruitment and training of radiologists. • Assess hormone receptor and HER2 status of biopsy samples in parallel. • Expand access to biomarker testing for BRCA and PD-L1 status.

Access to treatment

Challenges	Recommendations
• There is a very limited patient access to innovative cancer medicines. Only 5% of US FDA-approved innovative cancer medicine-indications were reimbursed locally in 2020, compared to 47% in Hong Kong and 61–63% in Australia, South Korea, and Taiwan. • Cancer medicines face considerable delays between regulatory approval and reimbursement. A recent analysis of innovative cancer medicine-indications with US FDA approval between 2010 to 2020 indicated that the local delay between regulatory approval and reimbursement may on average exceed 10 years. • Women may delay treatment due to trying alternative medicines first. The use of alternative medicines also during treatment with cancer medicines is common, with up to three fourths of breast or gynecological cancer patients using them, putting women at a risk of adverse drug interactions. • Around 24% of all cancer patients and their families face financial catastrophe, defined as out-of-pocket payments for medical services and non-medical services exceeding 30% of the annual household income.	• Enhance patient access to cancer medicines in the public sector. • Explore ways to include at least some cancer medicines with high clinical benefit more quickly in the national formularies, such as through managed entry agreements. • Health literacy among patients about the potential harms of alternative medicines taken without the knowledge of the treating physician needs to be improved. • Broaden current benefit packages of cancer care services in the public health insurance schemes to reduce unsustainable out-of-pocket payments.

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