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Unmasking Hidden Disparities: A Comparison of Female Breast Cancer Incidence, Mortality, and Management Strategy in China, the Republic of Korea, and Japan

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Abstract. Breast cancer remains the leading cause of cancer-related deaths among women worldwide, with significant variations in incidence and mortality across regions. It is the number one cancer among women in many Asian countries such as China, the Republic of Korea, and Japan. However, most of the articles analysed the data for Asia, especially these three East Asian countries as a whole. To explore whether the data from these three countries can be integrated, this study compared and summarized the similarities and differences in female breast cancer incidence, mortality, screening methods and available treatments between the three countries. We used estimated data from the Global Burden of Diseases (GBD) 2021 to compare the differences in breast cancer incidence and mortality between the three countries from 1990 to 2021. To compare the screening and treatment options, we summarized government and hospital guidelines for breast cancer treatment in countries. We found that the incidence in Japan was higher than China and Korea, and the increase over time has shown varying trends among countries. The mortality in China and Korea is stable, but in Japan older population continues to rise. Different screening and diagnostic methods available in each country may be related to the differences in breast cancer incidence and mortality. The study showed that there are similarities and differences in female breast cancer incidence and mortality as well as management strategies in these three countries. We would recommend future studies to evaluate these differences before conducting a pooled analysis in female breast cancer.

Keywords: Breast Cancer, China, the Republic of Korea, Japan

1. Introduction

Breast cancer is the most common fatal cancer among women in most countries. The World Health Organization (WHO) reported that 2.3 million women have been diagnosed with breast cancer and 670,000 have died globally in 2022 [1]. Compared to Western countries, many countries in Asia have higher incidence and mortality rates of breast cancer. Nearly half of the breast cancer patients were Asian by 2020 as reported by Sung et. al, and the Global Cancer Observatory (GCO) anticipated an annual increase of 1.5% from 2022 to 2040 in Asia [2, 3]. Thus, it is important to understand more about breast cancer management in Asia. Most of the articles studying breast

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cancer reports pooled data from multiple Asian countries, and overlooked the potential difference among different countries, especially the three East Asian countries. However, by looking at the studies and statistics separately for these three countries, there are differences in the breast cancer incidence and mortality. Breast cancer has leaded to about 416,000 new cases and over 117,000 deaths across China in 2020, with a median age of 45–49 years for new cases [4]. In Korea, the median age of breast cancer incidence is 45-49 years and the age-standardized incidence rate per 100k is about 59.9 [5]. While in Japan, it exhibits two peak ages for breast cancer, 45-49 and 60–64, and the incidence rate reached about 150 per 100k [6]. With social economic development and medical advances, the diagnosis and treatment of malignant tumors have improved over time, and the cure rate of early-stage cancer patients and the survival period of late-stage cancer patients have been lengthened as well [7].

In addition to epidemiological characteristics, these countries have different approaches to breast cancer screening, diagnosis and treatment. For screening, China favours self-testing for women starting at a young age (20 years old), Korea starts at 30 years old, and Japan at 40 [8-10]. As for breast cancer treatment, China favours conservative treatment for early-stage cancer (Stage 0 without many treatments), Japan favours conservative treatment for late-stage cancer (Stage III B/III C and Stage IV), and Korea's treatment is relatively more comprehensive at all stages [11-13].

More research is needed to see if pooling data from different countries in Asian for studying breast cancer is appropriate. To explore this question, here we will use three East Asian countries – China, Korea, and Japan – as case studies. We used data from the Global Burden of Diseases (GBD) 2021 report on Institute for Health Metrics and Evaluation (IHME) to compare the incidence and mortality of breast cancer among women, as well as their changes between 1990-2021, in these three countries, categorized by age. We will also study the available approaches for screening, diagnosis, and treatments in each country to understand the difference in breast cancer management.

2. Methodology

2.1. Data resources

Prepare your paper using clear and well written English. Poorly written English may obscure the scientific merit of your paper.

The data for this study were obtained from the GBD 2021 reports on female breast cancer in China, the Republic of Korea, and Japan from 1990 to 2021. We use the GBD 2021 database because it provides systematic comparisons of the severity of diseases, injuries and risk factors across age groups, gender, countries, regions and time. Because its large database covers 204 countries and territories, it provides a clear indication of trends in data at the national level [14]. GDB regularly updates the database, with each update re-estimating the complete period series data from 1990 onwards to ensure the highest level of completeness and comparability, reflecting real data trends [14]. For this study, data specifically related to female breast cancer in China, the Republic of Korea, and Japan was extracted, focusing on age-standardized incidence, age-standardized mortality and other indicators, analyzing the incidence and death of breast cancer in different years and age structures to ensure comparability across populations.

Screening, diagnosis, and treatment data were obtained from the ‘Breast Cancer Guidelines and Standards’ published by the Chinese Cancer Journal, the Nihon Keizai Shimbun, the National Cancer Research Center for Cancer Countermeasure Research, as well as from Daelim St. Mary's Hospital and the Korean Breast Cancer Foundation.

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2.2. Data visualization and statistical methods

This study used RStudio IDE (integrated development environment)for statistical computing and plotting [15]. A three-wire table was created to present the age-standardized mortality and incidence rates of breast cancer in the three countries. Additionally, six line charts were developed to illustrate trends in breast cancer incidence and mortality rates across three age groups, 20-39, 40-59, and 60-79 years. These visualizations were designed to highlight temporal trends and inter-country comparisons effectively. We used descriptive statistics to provide an initial overview of the data. We also conducted horizontal comparisons for time trend to look at differences in incidence and mortality rates across countries, as well as the time trend within each country.

3. Results

3.1. Age-standardized mortality and incidence of breast cancer in three regions (Table 1)

Starting from 1990, the overall female breast cancer average incidence rate in China has shown an upward trend in Table 1, while the average mortality rate shows a downtrend. However, the age-standardized mortality rate per 100k showed an upward trend from 1990 to 2004, when it reached its peak of 9.29 in the 1995-1999 period; from 2005 to 2019, the mortality rate began to decline, reaching its lowest in 2015-2019; and from 2019 to 2021, the rate began to rise again, finally reaching around 8. And the age-standardized incidence rate per 100k increases yearly from 18.59 in 1990-1994 to 32.55 in 2020-2021.

The average mortality rate per 100k of female breast cancer in Korea is showing an increasing trend, and the average incidence rate per 100k is showing a similar trend. Table 1 shows that in 1990-1994, the average mortality rate per 100k and incidence rate per 100k per year among Korean women were 5.36 and 13.82, respectively; while in 2020-2021, they increased to 6.22 and 38.53, respectively. Among them, the growth rate of the average incidence rate is significantly higher than that of the average mortality rate.

In Japan, the average mortality rate and the average incidence rate of breast cancer among women are also on the uptrend. During the period 1990-1994, the mortality and incidence rates per 100k were 7.74 and 35.17, respectively. Within 30 years, the incidence rate per 100k of breast cancer in Japan increased dramatically to 62.46, and the mortality rate also increased significantly to 10.28.

Table 1. Age-standardized mortality and incidence of female breast cancer in 3 countries (rate per 100k)

Period	China		The Republic of Korea		Japan	
	Mortality Rate	Incidence Rate	Mortality Rate	Incidence Rate	Mortality Rate	Incidence Rate
1990-1994	9.07	18.59	5.36	13.82	7.74	35.17
1995-1999	9.29	20.85	5.76	18.84	8.75	44.42
2000-2004	9.18	23.19	5.92	22.66	9.38	48.42
2005-2009	8.67	27.11	6.04	30.88	9.94	55.88
2010-2014	8.08	29.63	6.19	35.53	10.28	60.71
2015-2019	7.85	32.55	6.27	37.92	10.52	63.60
2020-2021	8.23	36.67	6.22	38.53	10.28	62.46

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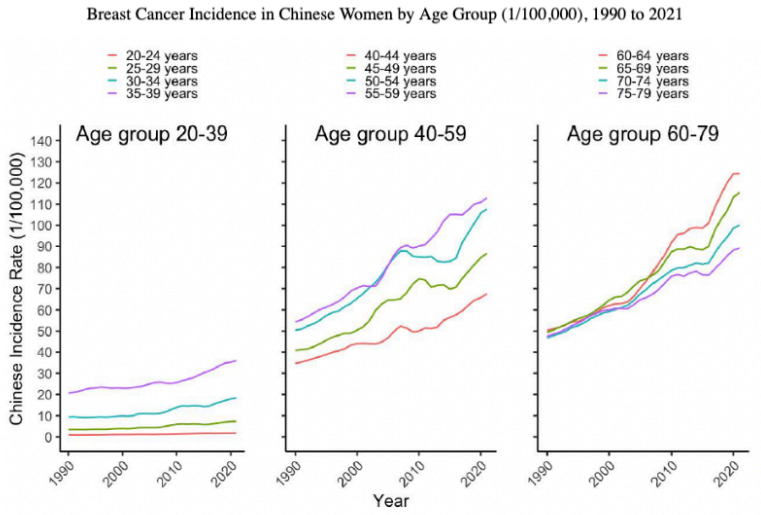
3.2. Female breast cancer incidence and mortality rates in three regions by age groups (20-39 years, 40-59 years, and 60-79 years)

In our study, females are categorised into three groups according to the common age of onset of breast cancer, 20-39 years, 40-59 years, and 60-79 years. Within these three groups, the chart further breaks it down into 5-year age gaps, and each group is further subdivided into 4 groups, totalling 12 age groups.

In China, age-specific trend analysis shows that the average incidence of breast cancer for all age groups shows an increasing trend from 1990 to approximately 2020 in Figure 1 (a). Breast cancer is virtually absent in females under 25 years old, and in the population over 25 years old, there is an overall trend of increasing incidence with age, peaking at 55-65 years and then decreasing with age. The average mortality rate, on the other hand, rises with age as shown by Figure 1 (b). Among women younger than 25 years show zero mortality from breast cancer, while the highest mortality rate (30-40) is reached at the age of 75-79 years.



(a) Breast cancer incidence (1/100,000) in China, 1990 to 2021

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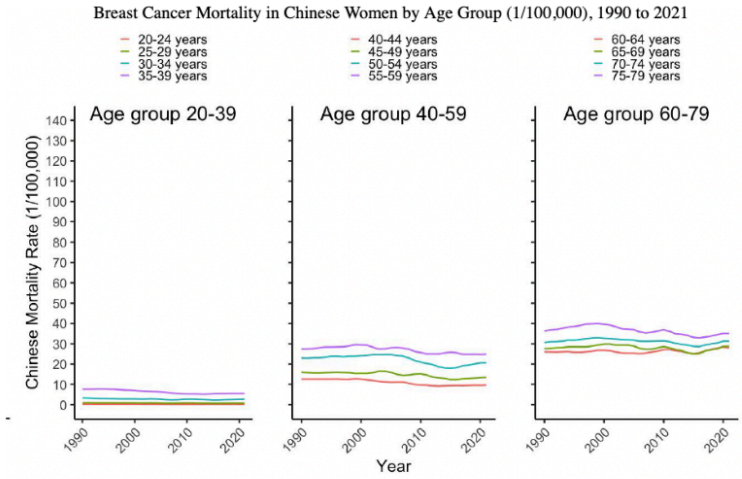
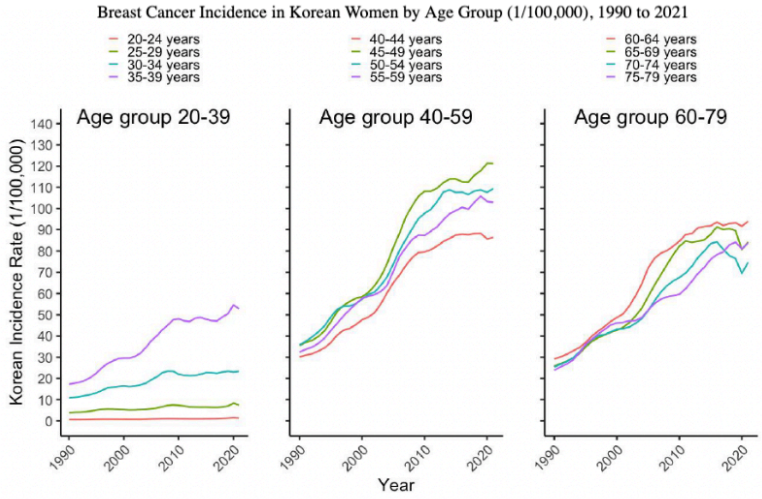


(b) Breast cancer mortality (1/100,000) in China, 1990 to 2021

Figure 1. Breast cancer incidence (a) and Mortality (b) in Chinese women by age group (1/100,000), 1990 to 2021

As shown in Figure 2 (a), women under 25 years in Korea have an incidence rate that is close to 0, and the probability of breast cancer in women older than 25 years of age gradually increases and peaks at 45-49 years and then gradually decreases. However, the average mortality per 100k figures vary much for women that's older than 45, with the average breast cancer mortality rates for women aged 45-74 all being very close to 10-20, while the rates are below 10 for those under 44. In Figure 2 (b), the highest mortality rate, over 20, is found in the 75-79 age group.



(a) Breast cancer incidence (1/100,000) in Korea, 1990 to 2021

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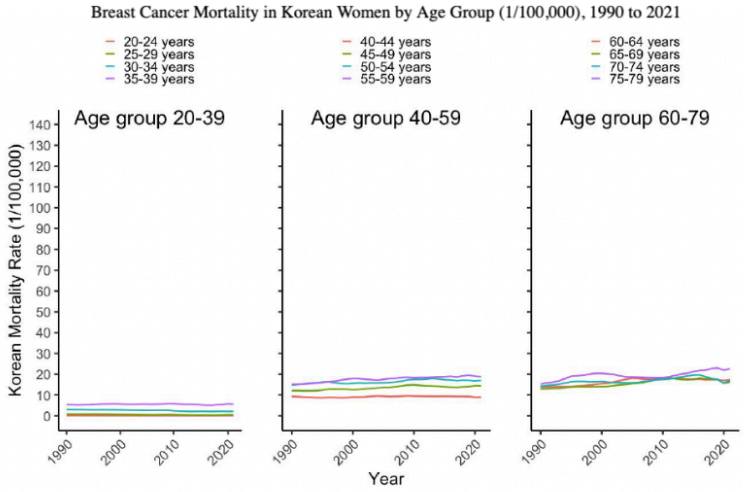
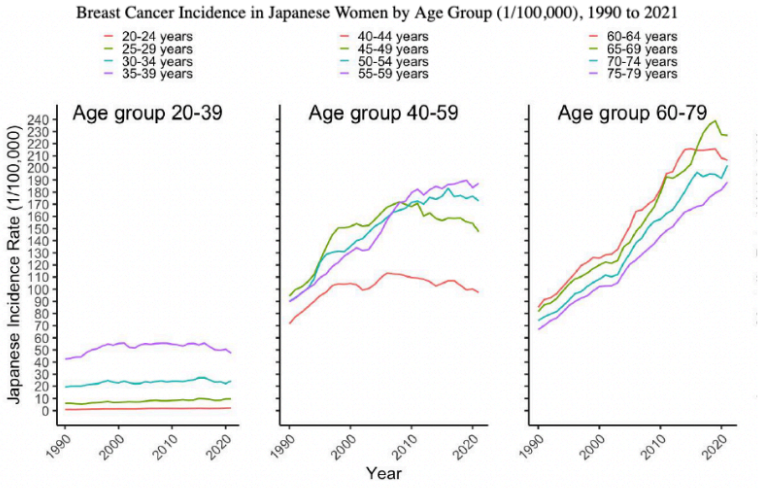


(b) Breast cancer mortality (1/100,000) in Korea, 1990 to 2021

Figure 2. Breast cancer incidence (a) and Mortality (b) in Korean women by age group (1/100,000), 1990 to 2021

The average incidence of female breast cancer in Japan is more complex. In Figure 3 (a), before 2010, the incidence rate was higher in women who were aged 45-59, while after 2010, 60-69 was called the age group with the highest incidence rate. Moreover, after 2010, the average incidence rate of the age group of 40-59 years old has been decreasing year by year. Before 2010, the 60-79 age group was very close to each other; after 2010, the 55-59 age group began to decrease year by year, while the 60-79 age group continued to increase and remained close to each other. Moreover, in figure 3 (b), the mortality rate for the 40-59, which was on the rise until 2000, turned around in the period 2000-2010 and has continued to show a downward trend ever since. For the 60-79, very close mortality rates and an increase all the way can be detected.



(a) Breast cancer incidence (1/100,000) in Japan, 1990 to 2021

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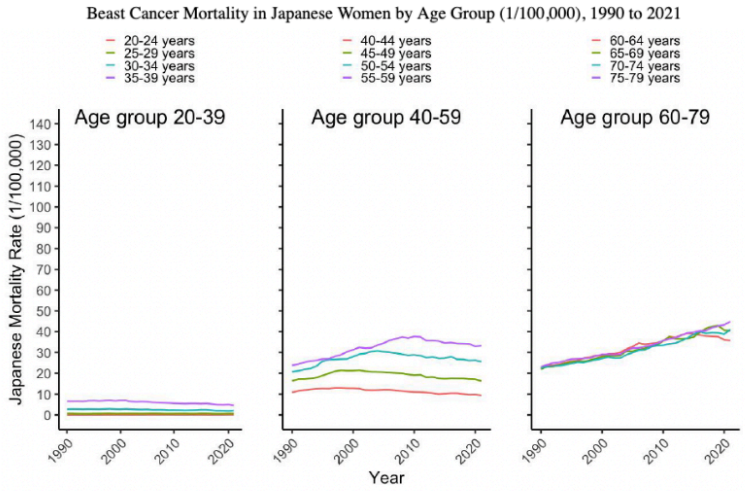

(b) Breast cancer mortality (1/100,000) in Japan, 1990 to 2021

Figure 3. Breast cancer incidence (a) and Mortality (b) in Japanese women by age group (1/100,000), 1990 to 2021

3.3. Screening guidelines and treatment options

3.3.1. Breast cancer screening guidelines in three countries, 2011 and 2022

We chose the years 2011 and 2022 because China released constructive breast cancer screening guidelines in 2011 to guide age-segmented screening everywhere. 2022 was chosen to compare changes in screening practices over the past 10 years. Neither Korea nor Japan has obviously changed their guidelines in the last 20 years, so the timing is aligned with China to facilitate comparison.

The guideline issued by the Breast Cancer Professional Committee of the Chinese Anti-Cancer Association in 2011 is the first time an age recommendation for early screening was included in the breast cancer treatment recommendations in China. Compared with the 2022 version, the age stratification in 2011 in Table 2 was very general, distinguishing only three age groups above 40 years old, and there was no clear distinction for the frequency of screening. Additionally, as shown in Table 2 and Table 3, Korea and Japan, in general have not changed much from the screening strategies implemented in 2022. Except for some detailed adjustments, for example, in 2011, clinical testing was recommended once every 1-2 years for women over 40 years of age in Korea, which was changed to once every 2 years in 2022.

Compared to 2011, the Breast Cancer Treatment Guidelines published by the National Health Commission of the People's Republic of China (NHRC) in Table 3, announcing that breast cancer screening generally begins after a woman is 20 in China. Women are encouraged to self-examine once a month after 20 and to undergo clinical examination every 1-3 years until the age of 30. After 40, it is recommended to begin mammography or ultrasound testing. In Korea, screening starts at a later age. Women are advised to start breast self-examination at age 30, clinical testing after age 35, and mammography after age 40. While in Japan, the starting age of screening is the latest. The recommended age for breast self-examination is set at 40, the same age as other screening methods, as Table 3 shown.

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Table 2. Age and frequency of breast cancer screening methods, 2011

Methods	China [16]	The Republic of Korea [17]	Japan [18]
Breast self-examination	>40	>30 once a month	>40 once every 2 years
Clinical examination	>40	35-40 once every 2 years >40 once every 1-2 years	\
Mammography	40-49 once a year 50-60 once every 1-2 years >70 once every 2 years	>40 once every 1-2 years	>40 once every 2 years
Breast ultrasound	>40 (for dense breast)	\	\
Medical interviews	\	high risk group once in a while	>40 once every 2 years

Table 3. Age and frequency of breast cancer screening methods, 2022

Methods	China [8]	The Republic of Korea [9]	Japan [10]
Breast self-examination	>20 once a month	>30 once a month	>40 once a month
Clinical examination	20-29 once every 1-3 years >40 once a year	>35 once every 2 years	\
Mammography	40-69 once every 1-2 years	>40 once every 1-2 years	>40 once every 2 years
Breast ultrasound	40-69 once every 1-2 years (for dense breast)	>40 once every 1-2 years	Suspected of having breast cancer
Medical interviews	\	\	>40 once every 2 years
Needle biopsy	\	Suspected of having breast cancer	Suspected of having breast cancer

3.3.2. Breast cancer treatment options in three countries, 2022

Treatment for women at different stages of breast cancer varies from country to country in 2022. In Table 4, women in China with early-stage breast cancer (Stage 0 to Stage II) are usually treated with surgery, radiotherapy, or a few chemotherapy treatments only, whereas for intermediate-stage (Stage III) patients, chemotherapy is used to supplement surgery, and palliative care is used for pain relief in advanced-stage (Stage IV) patients. For Korea, early-stage treatment is varied in Table 4. Compared with China, other than surgery, radiotherapy, hormone therapy, and chemotherapy are also recommended in Korea. Whereas the treatment for intermediate and advanced stage patients in Korea is softer than in China, with less surgery and more hormonal as well as pharmacological treatments for advanced stage patients. In Table 4, in Japan, treatment options are the same across stage 0 to stage II, with an emphasis on surgery, pathological diagnosis, radiotherapy, and medication. There are fewer treatments for patients with advanced stages in Japan compared with the options in the other two countries.

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Table 4. Treatment options of three countries, 2022

Stages	China [11]	The republic of korea [13]	Japan [12]
Stage 0	Surgery(lumpectomy or mastectomy); radiation therapy	Surgery(lumpectomy or mastectomy); radiotherapy; chemotherapy; hormone blockers; anti-HER2 drugs; combination therapy; neoadjuvant therapy	Surgery (mastectomy); sentinel lymph node biopsy; axillary lymph node dissection; histopathological diagnosis; radiation therapy; drug therapy
Stage I	Surgery (lumpectomy or mastectomy); adjuvant radiation; hormone therapy if hormone receptor-positive	Surgery(lumpectomy or mastectomy); radiotherapy; chemotherapy; hormone blockers; anti-HER2 drugs; combination therapy; neoadjuvant therapy	Surgery (mastectomy); sentinel lymph node biopsy; axillary lymph node dissection; histopathological diagnosis; radiation therapy; drug therapy
Stage II	Surgery; radiation therapy; adjuvant chemotherapy; hormone therapy if applicable	Surgery(lumpectomy or mastectomy); radiotherapy; chemotherapy; hormone blockers; anti-HER2 drugs; combination therapy; neoadjuvant therapy	Preoperative drug therapy; surgery (mastectomy); sentinel lymph node biopsy; axillary lymph node dissection; histopathological diagnosis; radiation therapy; drug therapy
Stage III A	Neoadjuvant chemotherapy followed by surgery; radiation therapy; adjuvant hormone therapy	Chemotherapy; hormone blockers; Surgery (lumpectomy or mastectomy); radiotherapy; chemotherapy; hormone blockers	Preoperative drug therapy; surgery (mastectomy); sentinel lymph node biopsy; axillary lymph node dissection; histopathological diagnosis; radiation therapy; drug therapy
Stage III B/III C	Neoadjuvant chemotherapy; surgery; radiation; systemic therapy	Chemotherapy; hormone blockers; Surgery (lumpectomy or mastectomy); radiotherapy; chemotherapy; hormone blockers	Drug therapy; surgery; radiation therapy
Stage IV	Palliative care; systemic therapy (chemotherapy, hormone therapy, targeted therapy); supportive measures	Hormone blockers or remove the ovaries (for estrogen receptor-positive tumours); chemotherapy; trastuzumab with pertuzumab (for HER2 receptor-positive tumours); radiotherapy	Drug therapy; surgery; radiation therapy

4. Discussion

4.1. Differences in female breast cancer-related data in three regions

The results of this study show that the age-standardized incidence rate and mortality rate of female breast cancer in China, Japan, and the Republic of Korea in 2021 have increased compared with those in 1990 among most of the age groups. The incidence rate of female breast cancer in China and South Korea was much lower than that of Japan in 1990-1994, and the trend was maintained in

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2020-2021. China's breast cancer age-standardized mortality rate was higher than Japan's in 1990-1994, but in 2020-2021 it will be lower than Japan's but higher than Korea's. Compared with the standardized mortality rate for both cancers in 1990, China's breast cancer mortality rate was higher than Japan's. Compared with 1990, the age-standardized incidence rates of female breast cancer in the three countries have increased respectively by 97.26%, 178.80%, and 77.59%, which is an obvious difference in the amplification.

The age-standardized incidence of breast cancer in women in the three countries showed similar trends over time. However, the trend of mortality rates was different across these three countries. This may be due to differences in healthcare systems, access to treatment, and demographic factors. Incidence rates have increased over the years in all three countries, with Japan continuing to have the highest incidence rate. However, China's incidence growth rate exceeded that of Korea and Japan from 2010 to 2021. The incidence rate in Japan has increased at a slower but stable rate, which may be attributed to the longstanding screening methods used in Japan and the aging of the population. Mortality rates show very different trends among the three countries. Japan has the highest mortality rate, which may be related to its ageing population (32.0 % of the female population is 65 or older in 2021) and limited treatment options for advanced cancer[19]. On the other hand, Korea has the lowest mortality rate, which may be due to its advanced and accessible healthcare system that can provide effective treatment for all stages of cancer. China has a mortality rate between Korea and Japan, but has improved in terms of early detection methods and advanced treatments.

4.2. Relationship between female breast cancer incidence and improved screening methods

The increasing incidence of breast cancer in China, Japan, and the Republic of Korea may be related to the development and implementation of improved screening methods in those regions. It is possible that early detection is related to increasing incidence but decreasing mortality. Early detection programs, especially mammography, breast ultrasound, and self-examination, have enabled more cases to be detected at an early stage of detection. The number of cases detected has increased as screening programs have become more widespread and improved, which is a possible reason for the increasing incidence in these three countries.

According to an analysis of the NHRC report, China updated and adjusted its breast cancer treatment guidelines in 2011 to include early breast cancer screening methods [16]. Therefore, the change in trend around 2010 may be due to more rational screening, which may be related to more early-stage patients being detected, lowering the mortality rate. The inclusion of mammography or ultrasound for women over 40 has led to an increase in the detection of early-stage cancers, which were previously underdiagnosed. As screening has become more sophisticated, more patients have been detected with the disease, and the incidence rate has been on the rise. Additionally, the 2022 updates to these guidelines have further refined age-specific screening recommendations, contributing to the upward trend in incidence rates.

Similarly, in the Republic of Korea, the national screening program promotes breast self-examinations starting at age 30 and mammography after age 40 [17]. These guidelines, introduced relatively earlier than in China, have enabled the detection of breast cancer in the 45-49 age group, which has the highest incidence rates. Japan’s strategies for screening, on the other hand, have remained essentially unchanged for over 30 years, with recommendations for self-examinations, mammography, and other methods beginning at age 40 [20]. This later starting age for screening may account for the higher incidence rates in older age groups, particularly those over 60. The

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country's focus on mammography and advanced imaging might have also contributed to the rise in incidence rates, as more cases are detected among older populations.

Of particular note, in Japan, the prevalence of patients in the 40-59 age group increased from 2000 to 2010, which was not observed in the other two countries. This may be because self-testing and other diagnostic requirements in Japan begin at age 40, leading to early detection of cancer in women in their 40s. In addition, the ageing of the population in Japan, which is the most severe of the three countries, may also be an important factor contributing to the decline in morbidity among young and middle-aged people in recent years [21]. The incidence of breast cancer in Japan has been higher than in the other two countries since 1990, and around 2020 it reached about 240 in the 65-69 age group, which is nearly twice as high as in the other two countries, but the incidence is more stable over time. This may be attributed to the fact that Japan started breast cancer screening earlier and has more statistics.

4.3. Relationship between female breast cancer mortality and treatment improvement

Treatment options across China, the Republic of Korea, and Japan show a difference in breast cancer care that has influenced mortality rates. All three countries use surgery, mainly lumpectomy or mastectomy, radiotherapy, and chemotherapy to treat breast cancer. The difference is that in China, the recommended treatment methods of early-stage breast cancer (stage 0, stage I, and stage II) are less than in the other two countries, and the treatment methods are more basic. In Japan, the treatment of breast cancer before stage III B/C is integral, but the treatment for stage III B/C and stage IV patients is very basic. Korea, in contrast, has a more sophisticated and rational treatment process compared to the other two countries.

In China, the incidence rate has been increasing since 1990, while there is a trend of decreasing mortality rate after 2000. This trend may be because of adding in more advanced screening, but challenges remain in ensuring access to effective treatments for patients. The author of the paper pointed out that China's increasing mortality rate may also be due to the country's rapidly grown population and the limited access to health care in parts of the country, especially in rural areas, as a result of uneven urban development [22].

Compared with China's breast cancer mortality rate over the past 30 years, Korea's mortality rate is not very different in trend. But the mortality rate for the 60-79 age group is very close to that for the 40-59 age group, unlike China, where the mortality rate for the 60-79 age group is nearly 10% higher than that for the 40-59 age group. In contrast to China, where palliative care is used to reduce the burden on patients with advanced disease, in Korea, the use of both drugs and surgery for patients with advanced disease might reduce the mortality rate of older women with the disease, as advanced cancer is more prevalent in the 60-79 age group. The systematic application of neoadjuvant therapies and targeted therapies in Korea has also potentially played a crucial role in improving survival rates.

In contrast to the other two countries, Japan's mortality rate for the 40-59 age group showed a turning trend from increasing to decreasing between 2000 and 2010, which was not seen in the other two countries. The 60-79 age group, on the other hand, has had a consistent upward trend in mortality over the last 30 years, but in general is numerically similar to the 40-59 age group. The decline in mortality among women aged 40-59 might be because the same turning trend in incidence that occurred between 2000 and 2010 resulted in fewer women with the disease and, as a result, fewer deaths. Moreover, the lack of treatment for seriously ill patients may contribute to the persistently high mortality rate among the elderly, since advanced stages are common among them.

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Long-standing treatments may not work well for older people, particularly as these patients may face age-related comorbidities and access to care.

5. Conclusion

This study comprehensively summarised the trends in breast cancer incidence and mortality among women in China, the Republic of Korea, and Japan from 1990 to 2021, utilizing data from the Global Burden of Diseases (GBD) 2021. The findings reveal that there are differences in breast cancer incidence and mortality rates and their changes over time across the three countries.

Trends in female breast cancer prevalence, and cancer age-standardized incidence and mortality are different in the three countries, and they may be influenced by screening and treatment programmes. What's more, China faces difficulties with the excessive size of the population and uneven medical conditions, while Japan's higher mortality rates among older populations reflect the need for more tailored interventions for aging demographics [21, 23]. These may also be a contributing factor to the change in trend. Future studies need to be aware of this difference before pooling data from these three countries or other countries in Asia, depending on what question they are trying to study.

However, this study has several shortcomings. The data of this study comes from GBD, in which the data are estimated data, which are not fully accurate statistics that may produce a part of error. In addition, the study did not compare the similarities and differences in breast cancer screening methods and medications used for breast cancer treatment in the three countries before 2011, due to the lack of reliable information released by official sources. These will require more accurate statistics and collation of data to improve the study in the future.

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