

NEW INCIDENCE TRENDS OF BREAST CANCER AND DIAGNOSTIC METHODS FOR HER2 IN VIETNAM IN YEAR 2010-2022

Le Thi Phuong^{1*}, Vu Thi Thu Hao^{2}, Nguyen Thi Hue³,
Ngo Van Lang⁴, Le Van Thu⁵, Duong Hong Quan⁵**

ABSTRACT

Aims: 1) Describe the trend in new incidence of breast cancer (BC) in the world and in Vietnam and 2) Describe the trend in diagnosis of HER2 in BC patients.

Materials and Methods: A number of studies and reports on the trend of cancer incidence of BC and diagnosis of HER2 in the period 2010-2022 in the world and in Vietnam. Synthesize and analyze data collected from 20 studies and articles on major online medical databases inclusive Medline/Pubmed, Web of Science, CI5 and GLOBOCAN; Domestic Medical Journal; Documents, Research Works, Thesis, Data Reported at International and Domestic Meeting. Zotero 6.0 software was used to manage and cite collected documents.

Results: 20 studies and reports in the world and in Vietnam were selected for the study, including seven documents on new trends of BC by time and geography, 13 documents on new trends for diagnosis of HER2. The incidence of BC tends to increase in the world and in Vietnam. Vietnam has a lower incidence rate than the world, but has a high mortality rate from cancer (10.5 deaths/26.4 new cases/100,000 population) equivalent to nearly 40%, common aged 50-59. Immunohistochemistry (IHC) is chosen as the routine test in the diagnosis of BC and FISH is the gold standard for evaluating HER2 gene amplification with a sensitivity of up to 98% with a specificity of 100%.

Conclusion: Vietnam is in the trend of increasing the incidence of BC in the world, mainly in the age group 50-59 during menopause, the mortality rate due to cancer is high, accounting for about 40% of all cases. new. The diagnosis of HER2 in BC is confirmed, the first test is IHC, FISH/CISH techniques.

Keywords: Breast cancer; HER2; diagnosis; Vietnam; IHC; FISH/CISH.

¹**Vinmec Times City International General Hospital;**

²**Bach Mai Hospital;**

³**Bac Giang General Hospital;**

⁴**Phenikaa University;**

⁵**Hanoi University of Public Health.**

*Corresponding Author: mlt2130067@studenthuph.edu.vn

**Corresponding Author: vuthuhao83@gmail.com

Date received: 22/3/2025

Date reviewed: 03/4/2025

Date accepted for publication: 10/4/2025

1. INTRODUCTION

Breast cancer (BC) is the most common cancer in women. It has surpassed lung cancer to become the leading cause of cancer worldwide, with 2.3 million new cases in 2022, accounting for 11.7% of all new cancer cases and 25.8% of all cancers in women. In Vietnam, it is estimated that there were 182,563 new cases and 122,690 deaths due to BC. For every 100,000 people, 159 are newly diagnosed, and 106 die from BC [1]. BC manifests in various subtypes. Advances in early diagnosis, intervention, and new treatment methods have improved survival rates and prognoses. Among these, targeted therapy has emerged as a key treatment option for HER2-positive BC patients. HER2 (Human Epidermal Growth Factor Receptor 2) is one of the four members of the EGFR (Epidermal Growth Factor Receptor) family, which includes four receptors: EGFR, HER2, HER3, and HER4. *HER2* gene amplification is observed in approximately 20–30% of BC patients. HER2-positive BC is a highly aggressive subtype characterized by an overexpression of the HER2 protein on the cancer cell surface beyond normal thresholds. This subtype tends to grow faster, metastasize earlier, and recur more quickly [2,3]. However, in Vietnam, no studies have yet addressed the trends in new BC diagnoses or the methods for diagnosing HER2 in patients. Therefore, we conducted this review with two objectives: 1) To describe the trends in new BC cases globally and in Vietnam. 2) To describe the trends in diagnostic methods for identifying HER2 in BC patients.

2. STUDY SUBJECTS AND METHODS

2.1. Study subjects

The study reviewed various research and reports on the trends in incidence, diagnosis, and treatment of breast cancer (BC) during the 2010-2022 period globally and in Vietnam.

2.2. Search strategy

2.2.1. Databases

Relevant studies were searched in medical databases such as Medline/PubMed, Web of Science, CIs and GLOBOCAN, as well as in domestic medical journals. Additional resources included research reports, theses, conference presentations and publications from both national and international sources. Data were updated until July 2022.

2.2.2. Search terms

English terms used for the search in titles or abstracts were: ([Breast cancer OR Breast carcinoma] AND [Incidence OR Epidemiology OR Epidemic OR Trend]) OR ([Breast cancer OR Breast carcinoma] AND [HER2 testing OR HER2 determination]).

2.3. Literature Selection

2.3.1. Inclusion Criteria

- Studies and reports with data published globally from 2010 to the end of July 2022.
- Studies and reports presenting BC incidence rates, including crude and age-standardized rates.
- Studies and reports on HER2 diagnostic techniques.
- Languages: English and Vietnamese.

2.3.2. Exclusion Criteria

- Studies and reports focusing on BC incidence in specific subpopulations rather than the general population.
- Studies and reports without clear population data for standardization.

2.3.3. Selection and Management Process

Literature from the databases underwent two rounds of classification:

- **Round 1:** Screening titles and abstracts, excluding studies based on the exclusion criteria.

- **Round 2:** Full-text review of articles that passed the first round. The Zotero 6.0 software was used for

managing and citing the collected literature.

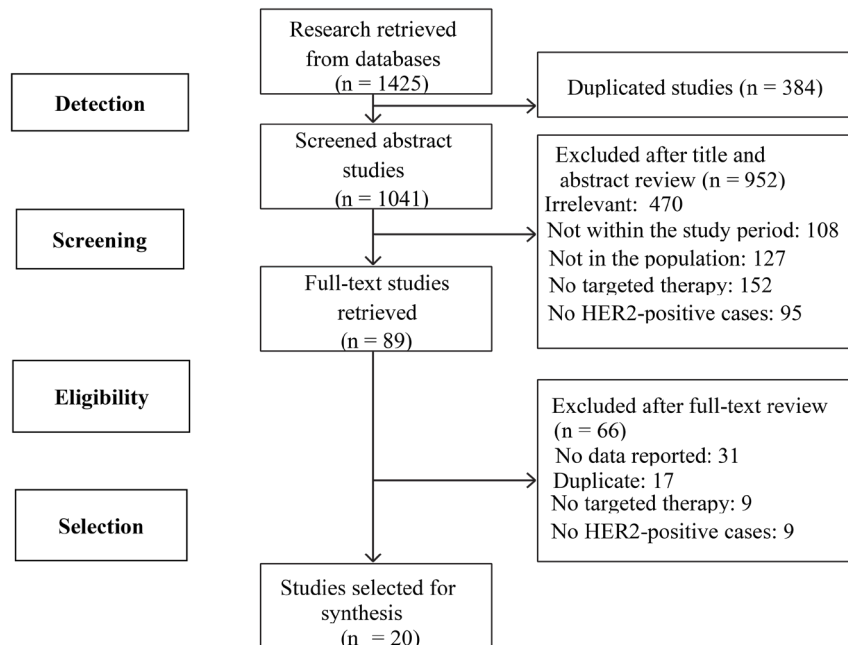


Figure 1. Search and selection results of studies

2.4. Screening results

Through comprehensive literature searches, 1,425 abstracts were identified from electronic databases that met the study's inclusion criteria. After removing 384 duplicates and excluding 952 studies that did not align with the objectives, population, or research issues, 89 full-text articles remained for further review. Of these, 66 articles were excluded due to the following reasons:

- No data reporting (31 articles).
- Duplication (17 articles).
- No targeted therapy (9 articles).
- No HER2-positive data (9 articles).
- Ultimately, 20 articles met the inclusion criteria for synthesis and analysis.

2.5. Characteristics of selected studies

According to Diagram 1, a total of 20 studies

were selected to present research findings based on two objectives, including 7 studies on the trends of new breast cancer incidence by time and geography and 13 studies on HER2 diagnostic trends.

2.6. Data Analysis

Data were analyzed using SPSS version 25 software (IBM, USA).

3. RESULTS

3.1. Trends in new breast Cancer incidence worldwide and in Vietnam

In 2020, the global incidence rate of breast cancer was 47.8 cases per 100,000 people, with Australia having the highest incidence rate at 95.5 cases per 100,000, while Southeast Asia had the lowest at 41.2 cases per 100,000 [1]. Moreover, the age-standardized incidence rate of breast cancer per 100,000 population showed an increasing trend, rising from 43.4 cases per 100,000 in 2012 to 47.8

cases per 100,000 in 2020. However, there were variations in incidence rates across different regions. Specifically, Australia had the highest incidence rate, increasing from 85.5 cases per 100,000 in 2012 to 94.2 cases per 100,000 in 2018 and 95.5 cases per 100,000 in 2020. Conversely, Southeast Asia had the lowest incidence rates over the years, recorded at 34.8, 38.1, and 41.2 cases per 100,000 in 2012, 2018 and 2020, respectively.

The rate of increase in new breast cancer incidence also varied across regions worldwide. North America experienced the highest increase, from 67.6 cases per 100,000 in 2012 to 89.4 cases per 100,000 in 2020, whereas Western Asia had the lowest increase, from 42.8 cases per 100,000 in 2012 to 46.6 cases per 100,000 in 2020 [1,4,5,6] (Figure 2).

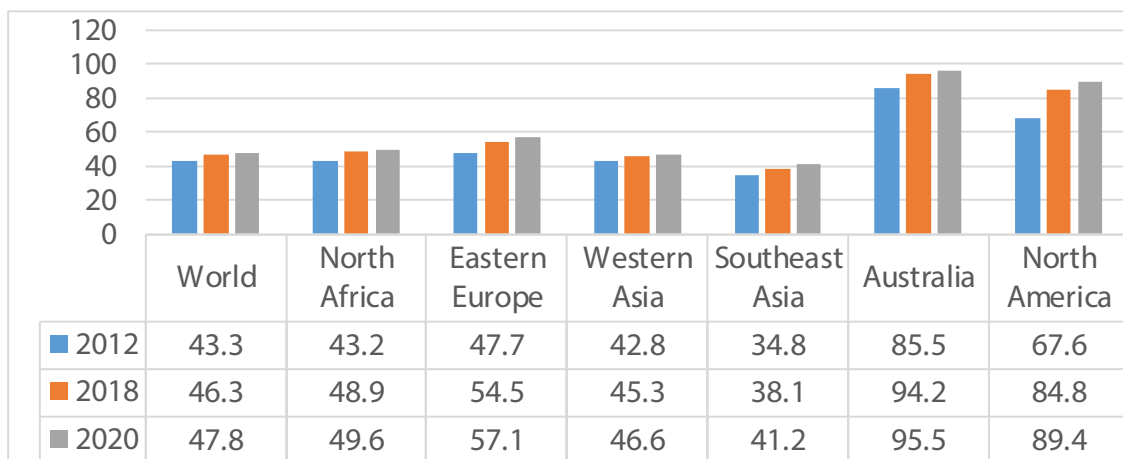


Figure 2. Age-Standardized Incidence Rates of Breast Cancer in Various Regions Worldwide [1, 4, 5, 6]

According to the report published in 2020, Vietnam recorded 21,555 new cases of breast cancer, accounting for 25.8% of all common cancers in women [7]. During the period from 2010 to 2020, the number of new cases showed an increasing trend over the years, with a sharp rise between 2018 and 2020, averaging approximately 3,163 new cases

per year. The age-standardized incidence rate per 100,000 population increased but was not consistent across the years. Specifically, in 2010, the rate was 29.9 cases per 100,000 population, which decreased to 26.4 cases per 100,000 in 2018 but then rose to 34.2 cases per 100,000 in 2020 (Table 1).

Table 1. New breast cancer incidence rates in Vietnam (2010-2020) [7]

Year	2010	2018	2020
Number of new cases	12,533	15,229	21,555
Age-standardized incidence rate per 100,000 population	29.9	26.4	34.2

The age group under 30 had the lowest incidence rate of breast cancer, specifically 1.5%, 1.3%, and

1.1% in 2014, 2016 and 2018, respectively. The highest incidence rate was observed in the 50–59

age group, with rates of 33.1%, 27.3%, and 34.8% in 2014, 2016 and 2018, respectively. The incidence rate of breast cancer increased with age, with the

highest concentration in the 50-59 age group, while cases were rare in those under 30 [2,8] (Table 2).

Table 2. New breast cancer incidence rates by age group (2014-2018) [2, 8].

Age Group	Year		
	2014	2016	2018
< 30	1.5	1.3	1.1
30-39	10.9	13.7	9.8
40-49	24.3	25.7	22.8
50-59	33.1	27.3	34.8
60-69	22.3	21.5	31.5
>70	7.9	10.5	

3.2. Trends in HER2 diagnosis in breast cancer patients

Different HER2 diagnostic techniques for breast cancer patients have their own advantages and limitations. Immunohistochemistry (IHC) can only detect protein expression on the cell membrane, while gene and protein expression are not always consistent. Therefore, FISH/CISH techniques have been implemented to accurately assess the amplification level of the *HER2* gene.

The issue of specimen collection is also a concern in simplifying the process. In previous techniques such as IHC and FISH/CISH, most tests were performed using paraffin-embedded tissue samples. However, tissue samples have certain limitations and cannot be repeatedly tested multiple times. Therefore, future techniques are being developed to use blood samples, such as the ELISA method [9] (Table 3).

Table 3. HER2 Diagnostic Techniques [2, 9]

No.	Diagnostic Technique	FDA Approved	Method	Sample Type	Target	Advantages	Disadvantages
1	IHC CTA	No	IHC (CB-11 + 4D5 antibody)	Paraffin-embedded tissue	HER2 protein on the cell surface	Simple, low cost	Affected by factors such as fixation time and method; subjective due to semi-quantitative scoring
2	IHC HerceptTest	Yes	IHC polyclonal goat antibody)				
3	IHC Pathway	Yes	IHC (CB-11 replaced with 4B5 in 2008)				

No.	Diagnostic Technique	FDA Approved	Method	Sample Type	Target	Advantages	Disadvantages
4	FISH Inform	Yes	FISH (HER2 probe)	Parafin-embedded tissue	HER2 gene on chromosome 17	More accurate than IHC, less affected by pre-analytical factors	Higher cost and more time-consuming than IHC
5	FISH PathVysion	Yes	FISH (HER2 + CEP17 probe)				
6	FISH HER2 PharmDX	Yes	FISH (HER2 + CEP17 probe)				
7	CISH Spot-Light	Yes	FISH (HER2 probe)	Parafin-embedded tissue	HER2 gene on chromosome 17	Lower cost and faster than FISH; easy signal assessment	Difficult to evaluate in areas with high amplification levels
8	SISH Enzmet	No	FISH (HER2 + CEP17 probe)			Fully automated, easy signal assessment	Requires additional hybridization to evaluate CEP17 separately to overcome chromosome 17 polysomy
9	mRNA OncoTyeDX	No	RT-PCR	Fresh/frozen tissue	mRNA	Can assess RNA levels and quantify expression	False negatives due to RNA degradation in tissue samples
10	mRNA	No	RT-PCR; microarray				
11	Dimerization HERmark	No	VeraTag capillary electrophoresis	Parafin-embedded tissue	Protein dimers	Simple, accurate, quantifiable	Expensive and time-consuming
12	ELISA serum HER2 Advia Centaur	Yes	Sandwich immunoassay	Serum sample	Protein (serum)	Easy to perform, fast, uses serum samples	Results may be affected in patients undergoing Trastuzumab treatment

4. DISCUSSION

Globally, the incidence of breast cancer has shown an increasing trend across all regions. However, the rate of increase varies among continents. In 2020, Australia had the highest incidence rate, with 95.5 cases per 100,000 population, while Southeast Asia had the lowest, with 41.2 cases per 100,000 [1]. From 2012 to 2020, North America experienced the highest increase in new breast cancer cases, with a growth rate of 21.8 cases per 100,000 population. This suggests that breast cancer incidence is influenced by various factors, including socioeconomic conditions, lifestyle, cultural habits and exposure to carcinogens.

Furthermore, developed countries tend to have high breast cancer incidence rates but significantly lower mortality rates (Australia: 12.1 deaths per 100,000, North America: 12.5 deaths per 100,000) [1]. This reflects the fact that while lifestyle factors in these countries—such as processed food consumption, low birth rates, and short breastfeeding duration—may contribute to an increased risk of breast cancer, their advanced healthcare systems ensure effective early screening, diagnosis, and treatment, leading to higher early detection rates and lower mortality.

Conversely, in regions like North Africa and Western Asia, women's health issues are often overlooked, making breast cancer a leading cause of mortality due to late-stage detection. Notably, approximately 20% of breast cancer cases worldwide are attributed to modifiable risk factors, including alcohol consumption, smoking, obesity, and physical inactivity. Therefore, reducing the burden of breast cancer requires promoting healthier lifestyles and habits.

Vietnam follows a similar trend of increasing breast cancer incidence as seen globally. Between 2010 and 2020, the incidence rate rose from 29.9 to 34.2 cases per 100,000 population. Although Vietnam does not belong to the group of countries

with the highest incidence rates and has a lower incidence rate than the global average, it has a high breast cancer mortality rate (10.5 deaths per 26.4 new cases per 100,000 population), equivalent to nearly 40% [6]. This high mortality rate may be due to late-stage diagnosis, poor prognosis, and ineffective treatment. Therefore, breast cancer screening and early detection are crucial, as early-stage diagnosis leads to simpler treatment, higher treatment efficacy, and lower costs.

Immunohistochemistry (IHC) is the most widely used diagnostic method for determining HER2 protein overexpression on breast cancer cell surfaces, with approximately 80% of breast cancer patients in the U.S. diagnosed with HER2 status using IHC. IHC has advantages such as simplicity, ease of implementation, low cost, and broad applicability in diagnostic laboratories. However, IHC results rely on a semi-quantitative scoring system, which introduces subjectivity and reduces accuracy.

To overcome these limitations, fluorescence in situ hybridization (FISH) is used to detect HER2 gene amplification through fluorescently labeled probes. FISH can incorporate chromosome 17 centromere (CEP17) probes for quality control. Currently, three FDA-recommended FISH techniques with equivalent diagnostic value include FISH Inform, which detects HER2 alone and FISH PathVysion and FISH PharmDX, which use dual probes for HER2 and CEP17 centromere detection. Among these, FISH is considered an objective scoring method, offering high accuracy in detecting *HER2* gene amplification, making it the gold standard with a sensitivity of 98% and a specificity of 100% [9]. When IHC results are equivocal (IHC 2+), additional FISH testing is required for confirmation. However, FISH has some drawbacks, including the need for a fluorescence microscope, higher costs and longer processing times compared to IHC.

The introduction of chromogenic in situ hybridization (CISH) and silver-enhanced in situ hybridization (SISH) has integrated the advantages of both IHC and FISH. These methods detect *HER2* gene copy number using a single *HER2* probe labeled with chromogenic or silver stains, eliminating the need for fluorescence microscopy. CISH and FISH have shown a high concordance rate of 97–99% [9].

In Vietnam, IHC remains the first-line diagnostic test for determining *HER2*-positive breast cancer. If the IHC result is 2+, confirmatory FISH/CISH testing is required.

5. CONCLUSION

Vietnam is experiencing an increasing trend in new breast cancer cases, similar to the global pattern. The disease is most commonly diagnosed in women aged 50–59 during menopause, and the mortality rate is high, accounting for approximately 40% of new cases. The primary diagnostic test for *HER2*-positive breast cancer is IHC, with FISH/CISH used for confirmation when the IHC result is 2+, offering a sensitivity of 98% and a specificity of 100%.

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