Cancer Innovation

CANCER INNOVATION

CLINICAL GUIDELINE OPEN ACCESS

Guideline for the Management Pathway and Quality Control of Breast Cancer Prevention and Treatment in China's Counties

Breast Cancer Expert Committee of National Cancer Quality Control Center | Cancer Prevention and Treatment Committee of Healthy China Research Center

Correspondence: Fei Ma (drmafei@126.com) | Binghe Xu (xubingheBM@163.com)

Received: 27 November 2024 | **Accepted:** 10 December 2024

Funding: The authors received no specific funding for this work.

Keywords: breast cancer | county-level | prevention and treatment management | quality control

ABSTRACT

Breast cancer is one of the most common malignant tumors among women in China, with approximately 306,000 new cases reported in 2016. Notably, around 33% (100,400) of these cases occurred in rural areas. County-level hospitals, encompassing counties and county-level cities, serve as the primary diagnostic units for the majority of rural breast cancer patients. These hospitals are integral to cancer prevention, screening, maintenance treatment, rehabilitation, follow-up, and referral processes. However, economic and geographical constraints result in county-level hospitals being relatively deficient in medical equipment, health human resources, and drug accessibility. Consequently, there is a critical need for breast cancer prevention and management guidelines that are tailored to the specific conditions of China's counties. In response to this need, and within the policy framework of hierarchical diagnosis and treatment, a Chinese expert group has developed the *Guideline for the Management Pathway and Quality Control of Breast Cancer Prevention and Treatment in China's Counties (2023 Edition)*. This guideline aims to expand the availability of quality medical resources, ensure better distribution of these resources across regions, and enhance the capacity for breast cancer prevention and treatment. Ultimately, the goal is to improve the prognosis and quality of life for breast cancer patients in China's counties. This guideline includes clear and concise path diagrams that are easy to implement in clinical practice, serving as a valuable reference for clinicians in county-level hospitals.

1 | Introduction

Breast cancer is the leading malignancy threatening the health of women in China. According to data from the China National Central Cancer Registry, approximately 306,000 new cases of breast cancer were diagnosed in Chinese women in 2016, representing 16.7% of all malignant tumor cases. Of these, around 33% (100,400) were reported in county areas, including rural regions [1]. County-level hospitals, encompassing both counties and county-level cities, serve as the primary diagnostic centers for most rural breast cancer patients. These hospitals are integral to health education, screening, maintenance treatments, follow-ups, and referrals.

In 2018, the Breast Cancer Expert Committee of the National Cancer Quality Control Center was established to enforce quality control measures in breast cancer diagnosis and treatment. The committee's goal is to standardize diagnostic and treatment

Abbreviations: AI, aromatase inhibitor; BI-RADS, Breast Imaging Reporting and Data System; ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; HR, hormone receptor; PR, progesterone receptor; TNBC, triple-negative breast cancer.

practices, promoting national standardization, homogenization, and normalization, ultimately aiming to improve the survival rates and quality of life for breast cancer patients nationwide. Several guidelines have been published to support this mission, including the *Guideline For Rational Medication of Breast Cancer* [2], *Guidelines for Breast Cancer Screening and Early Diagnosis and Treatment in China (2019 Edition)* [3], and *Quality Control Index for Standardized Diagnosis and Treatment of Breast Cancer in China (2022 Edition)* [4]. These documents provide comprehensive protocols covering various aspects such as screening, early diagnosis and treatment, standardized clinical procedures, rational medication, and posttreatment follow-up and monitoring.

Previously, the National Health Commission of the People's Republic of China launched the *Thousand County Projects Work Plan to Improve Comprehensive Capabilities of County-level Hospitals (2021–2025)* [5], which aims to elevate at least 1000 county hospitals to the medical service level of tertiary hospitals by 2025. However, many county-level hospitals face economic and geographical constraints, resulting in deficiencies in medical equipment, personnel, and drug accessibility. This situation underscores the urgent need for breast cancer prevention and management guidelines tailored to the specific circumstances of county hospitals, supplementing the existing guidelines and protocols.

In response, the National Cancer Center and National Cancer Quality Control Center have tasked the Breast Cancer Expert Committee with convening clinical experts from core and county hospitals to draft the *Guideline for the Management Pathway and Quality Control of Breast Cancer Prevention and Treatment in China's Counties (2023 Edition)*. This guideline aims to promote the expansion and equitable distribution of high-quality medical resources, advancing the frontline of breast cancer prevention and control. The guideline adheres to scientific and standardized principles, fully considering the realities of breast cancer diagnosis and treatment in county-level hospitals, and strives to be both universal and operable. In developing the quality management and control framework, experts referenced the 12 breast cancer quality control indicators in the *Professional Quality Control Indicators for Oncology (2023 Edition)* [6] issued by the National Health Commission in 2023. The expert opinions were derived from targeted discussions among the guideline writing committee members, all of whom reported no conflicts of interest.

2 | The Management Pathway of Breast Cancer Prevention and Treatment in Counties

2.1 | Breast Cancer Hierarchical Diagnosis and Treatment Pathway in Counties

In China, the hierarchical diagnosis and treatment system plays a crucial role in managing the vast population and the high incidence of breast cancer, helping to prevent the overcrowding of medical resources and optimize their utilization. China has 2844 county-level administrative regions, where county-level hospitals serve as public healthcare institutions established in counties, county-level cities, municipal districts, and banners. These hospitals are integral to the rural three-tier medical and health service network and act as a bridge between urban and rural healthcare systems [7, 8]. As of the end of 2022, 45.6% of county hospitals had reached the capacity of tertiary hospitals, and 87.7% had achieved the capacity of secondary hospitals [9]. Despite the steady improvement in the medical service levels of county-level hospitals, there remains a need for continuous enhancement in tumor prevention and control management. County-level hospitals that have attained the diagnostic and treatment capabilities of tertiary hospitals and are equipped with complete facilities are considered equivalent to higher-level hospitals under this guideline. The primary focus of this guideline is on county-level hospitals that have not yet reached the diagnostic and treatment level of tertiary hospitals. These hospitals should prioritize breast cancer prevention, screening, follow-up, monitoring, maintenance treatment, and rehabilitation for women in counties and townships. The guideline is developed in accordance with the Technical Program for Hierarchical Diagnosis and Treatment of Breast Cancer issued by the National Health Commission [10], taking into account the different functional roles and division of labor of medical institutions at various levels in the breast cancer prevention and control process. See Figure 1 for the formulation of Breast Cancer Hierarchical Diagnosis and Treatment Path in counties.

County-level Guideline Recommendation 1: County hospitals bear the primary responsibility for health education, screening, primary diagnosis and treatment, maintenance treatment, management of adverse reactions to antitumor drugs, patient follow-up, recurrence monitoring, rehabilitation guidance, and two-way referrals for breast cancer. When county hospitals lack the necessary diagnostic and treatment capabilities or medical technical conditions, timely referrals should be made to county-level or higher-level hospitals equipped with the required resources. County-level hospitals with

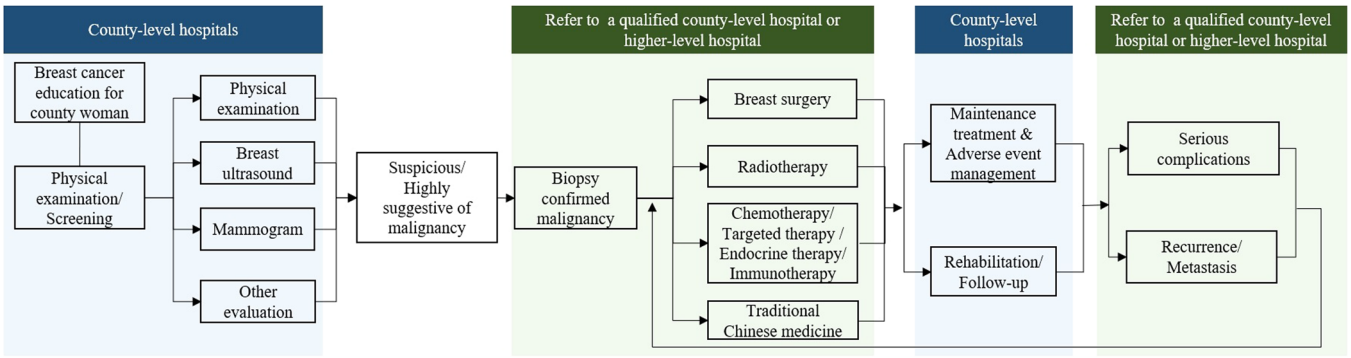

FIGURE 1 | Breast cancer hierarchical diagnosis and treatment pathway in counties.

the requisite conditions and capabilities can also perform breast cancer surgeries, radiotherapy, chemotherapy, targeted therapy, endocrine therapy, immunotherapy, clinical research, and other related activities. All diagnostic and treatment pathways outlined below are based on this principle of referral.

2.2 | The Content of County-Level Breast Cancer Popular Science Education

2.2.1 | The Prevention of Breast Cancer

Breast cancer prevention is categorized into three levels. Primary prevention, also known as etiological prevention, aims to avert the onset of breast cancer by controlling causes or risk factors. It represents the most proactive and fundamental preventive measure. By understanding the relevant causes of breast cancer, corresponding interventions can be implemented to reduce its incidence at its source, minimize patient harm, and alleviate the anticancer burden on individuals and society. Epidemiological data indicate several high-risk factors for breast cancer, some of which can be mitigated through public education, such as obesity, unhealthy dietary patterns, smoking, and alcohol consumption [11]. County-level healthcare professionals should inform residents about maintaining a healthy weight, engaging in regular exercise, adopting a balanced diet, and quitting smoking and alcohol. Specific recommendations include the following: (1) Healthy diet: Increase the intake of dietary fiber and soy products, limit the consumption of high-sugar and high-fat processed foods, and minimize processed meat consumption. (2) Regular exercise: To boost immune function and reduce body fat percentage. Exercise should commence early, ensuring a weekly duration of 150–300 min for moderate-intensity exercise or 75–150 min for high-intensity exercise, particularly for high-risk populations with BRCA1/2 gene mutations. (3) Quit smoking and alcohol. However, some high-risk factors are uncontrollable, such as age, family history of breast cancer, and BRCA gene mutations. These factors can be actively addressed through secondary prevention. Secondary prevention involves early detection, diagnosis, and treatment, aiming to discover disease clues early, prevent or slow disease progression and deterioration, and improve cure rates and survival rates. The primary measure is early screening, especially for specific high-risk populations, which significantly reduces their incidence and mortality rates. Regular self-examination for visible and palpable areas is also recommended to be aware of potential signs of breast cancer [11]. Tertiary prevention, or recovery prevention, primarily provides various treatment measures for diagnosed patients to improve survival and recovery rates. This includes preventing tumor recurrence and metastasis and reducing postoperative pain and other complications. Currently, various treatment guidelines for breast cancer fall broadly within the scope of tertiary prevention [11]. Measures for secondary and tertiary prevention will be detailed in the screening and treatment sections of this guideline and are not reiterated here.

2.2.2 | Clinical Manifestations of Breast Cancer

Most breast cancers initially present as painless lumps, with only a few cases involving varying degrees of dull pain or tingling. Additionally, some patients may experience nipple discharge, which is typically bloody and watery. As the disease progresses, patients may develop skin changes, nipple retraction, and palpable enlarged lymph nodes in the axilla [12].

2.2.3 | Breast Self-Examination

While breast self-examination does not reduce the incidence rate of breast cancer, it can significantly enhance health awareness among residents and promote early diagnosis and treatment of breast diseases. In areas with limited medical resources, breast self-examination can help reduce the risk of locally advanced breast cancer. Therefore, medical staff should educate residents on the proper technique for performing breast self-examination [13].

Self-examination Timing: Premenopausal women should perform self-examination 7 to 14 days after menstruation, while postmenopausal women should choose a fixed date each month.

Self-examination Methods: (1) Look: Stand in front of a mirror with your upper body straight and your hands on your waist. Observe the size and shape of both breasts for any changes. Check for redness, rashes, wrinkles, depressions, or “orange peel” changes on the skin, as well as any changes in the nipples, such as raising, retraction, or discharge. Also, look for any bulges in the bilateral axilla. Raise your hands high and observe for any of the above changes again. (2) Touch: Lie on your back, place four fingers flat together on the breast, and move them up and down to examine the entire breast. Make circular movements with your fingers at each location. Use gentle force to examine the skin and subcutaneous tissue, moderate force to examine the middle gland, and strong force to press the breast gland against the chest wall to examine deep tissue and feel the thoracic cage. Repeat the examination on the contralateral breast with both hands. Stand up and recheck using the same method. Check each location for any lumps or other changes, along with lymph nodes in the axilla. Gently squeeze the nipple with the thumb and index finger to check for any discharge.

2.2.4 | Screening for Breast Cancer

Screening methods for breast cancer include mammography, ultrasound, and, if necessary, MRI. Given the limited penetration of X-rays in dense breast tissue and considering the characteristics of Asian women's breasts, ultrasound can be employed as a routine screening modality. MRI, while highly accurate, is costly and is recommended as a supplementary tool to mammography and ultrasound [14].

2.2.5 | Diagnosis and Treatment of Breast Cancer

The diagnosis of breast cancer necessitates a pathological confirmation, with histological specimens obtainable via fine-needle aspiration or excisional biopsy, with fine-needle aspiration being the preferred initial method in adequately

equipped hospitals. It is imperative to inform patients suspected of having breast cancer that there is no current evidence suggesting that a biopsy will lead to metastasis [14]. Breast cancer treatment options include surgery, radiotherapy, chemotherapy, targeted therapy, endocrine therapy, and traditional Chinese medicine. Ensuring that patients are aware of standardized treatment protocols and fostering confidence in these treatments is crucial for managing breast cancer as a chronic, manageable condition.

2.3 | Screening Pathway for Breast Cancer in County Areas

Breast cancer screening aims to identify and detect precancerous lesions with progressive potential and early invasive cancer in asymptomatic women through effective, simple, and economical breast examination measures. The objective is to facilitate early detection, diagnosis, and treatment, ultimately reducing the mortality rate of breast cancer in the population.

For individuals at average risk, it is generally recommended that breast cancer screening commence at the age of 40, with a screening frequency of once every 1–2 years [12, 14]. For high-risk individuals—those with a clear genetic predisposition to breast cancer, a history of breast ductal/lobular dysplasia or lobular carcinoma in situ (LCIS), or those who have undergone thoracic radiotherapy—screening should be initiated before the age of 40, with a recommended frequency of once per year. Screening methods may include breast ultrasound, X-ray examination, and, if necessary, advanced imaging techniques such as breast MRI [12, 14].

This screening pathway is informed by the *China Guideline for the Screening and Early Detection of Female Breast Cancer (2021, Beijing)* [15] and the *Screening and Early Diagnosis of Breast Cancer in China: A Practice Guideline (2022 Edition)* [16] issued by the Society of Breast Cancer China Anti-cancer Association. The county-level breast cancer screening pathway is illustrated in Figure 2.

County-level Guideline Recommendation 2: Given the relative paucity of county-level and primary medical resources in China, breast ultrasound should be the preferred screening modality for breast cancer in these areas. Concurrently, coordination of human and material resources through remote imaging, mobile screening vehicles, and other means should be considered to bolster screening efforts at the county and grassroots levels.

3 | County-Level Breast Cancer Diagnosis Pathway

The diagnostic pathway for breast cancer is illustrated in Figure 3. Diagnosis should integrate patients' clinical manifestations, imaging examinations, histopathology, and other relevant factors. Figures 4–6.

3.1 | Clinical Manifestations

Early symptoms and signs of breast cancer may be overlooked by patients. Physicians in county-level hospitals must be vigilant for typical indicators of breast cancer during consultations and physical examinations. Key signs include breast lumps, nipple discharge, skin depression of the breast, nipple and areola abnormalities, and enlarged axillary lymph nodes. The optimal time for premenopausal women to conduct breast lump examinations is after the menstrual period. Additionally, attention should be given to symptoms and signs from other organ systems, such as bone, lung, liver, and brain, which may indicate breast cancer metastasis [14].

3.2 | Imaging Examination

Breast X-ray, ultrasound, or MRI should be performed on the breast and regional lymph nodes, including the axilla and the upper and lower clavicular regions. Following a breast cancer diagnosis, additional imaging assessments are required to identify potential distant metastases based on clinical indications. A chest CT scan is recommended for patients with confirmed breast cancer, particularly those with late-stage tumors and a high risk of recurrence. In patients with confirmed cancer, an abdominal ultrasound should be performed initially, with abdominal CT or MRI performed when organ metastases are suspected. For patients with a stage higher than T3N1M0 and rapidly progressing disease, a bone radionuclide scan is advised. This scan is also recommended for routine initial

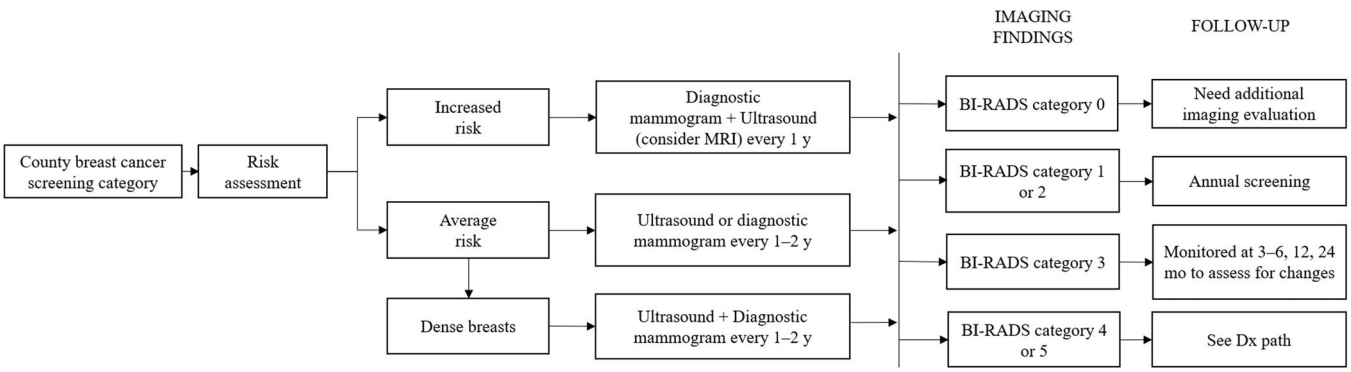

FIGURE 2 | County-level breast cancer screening pathway. BI-RADS, Breast Imaging Reporting and Data System.

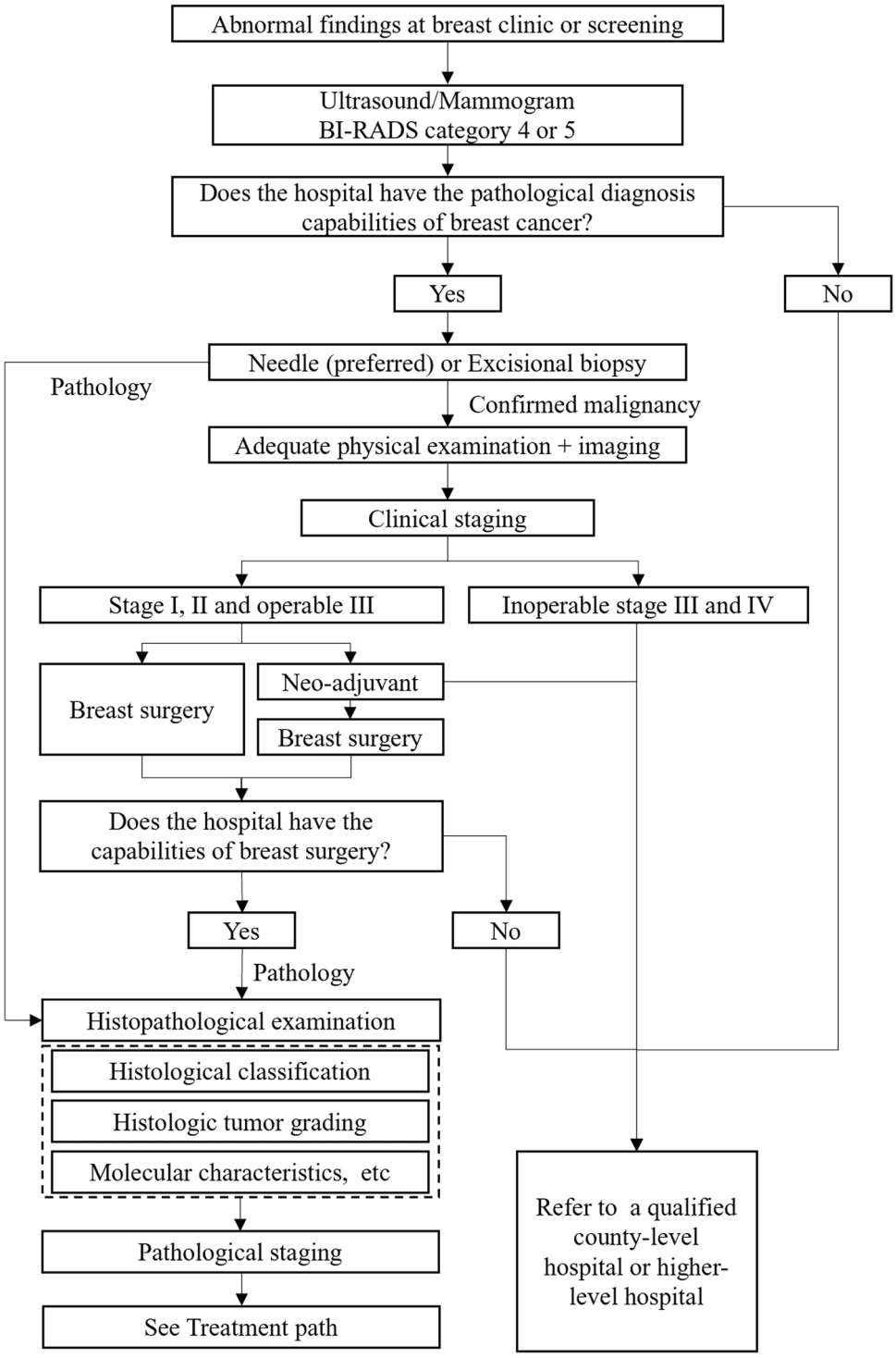

FIGURE 3 | County-level breast cancer diagnostic pathway. BI-RADS, Breast Imaging Reporting and Data System.

screening in cases of suspected bone metastasis, such as bone pain, fractures, elevated alkaline phosphatase, and hypercalcemia. While cranial CT or MRI can be useful in detecting asymptomatic brain metastases, it is not routinely recommended. PET-CT is generally not recommended for routine evaluation but may be considered when results from other tests are inconclusive or raise suspicion. Imaging examinations are crucial for the clinical TNM staging of breast cancer and must be completed before initiating treatment.

3.3 | Histopathological Examination

Pathological diagnosis is the gold standard for breast cancer diagnosis, significantly influencing the selection of treatment regimens and the prediction of efficacy and prognosis. It is essential to obtain a pathological diagnosis before commencing antitumor drug therapy. A standardized pathological diagnosis report for breast cancer should not only confirm the benign or malignant nature of breast lesions but also provide the following essential

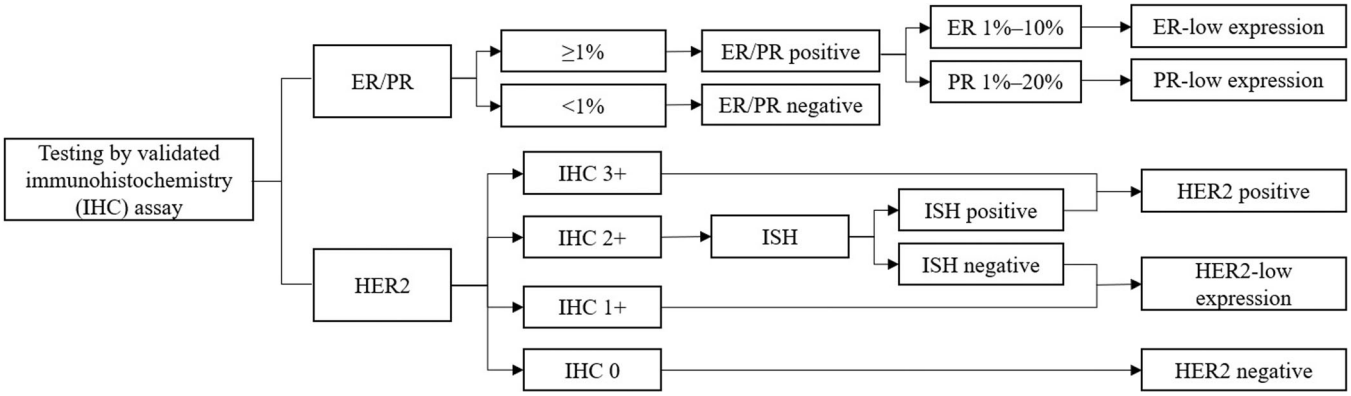

FIGURE 4 | Interpretation of ER/PR and HER2 status. ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; ISH, in situ hybridization; PR, progesterone receptor.

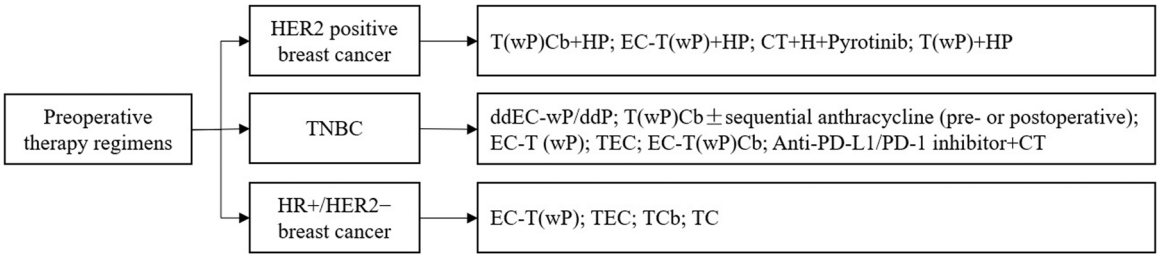

FIGURE 5 | County-level neoadjuvant treatment pathway for breast cancer. ddEC, dose-dense epirubicin plus cyclophosphamide; ddP: dose-dense paclitaxel; EC-T, epirubicin plus cyclophosphamide followed by docetaxel; H, trastuzumab; HER2, human epidermal growth factor receptor 2; HP, trastuzumab plus pertuzumab; HR: hormone receptor; PD-L1: programmed death-ligand 1; PD-1: programmed death receptor 1; TC, docetaxel plus cyclophosphamide; TCb, docetaxel plus carboplatin; T(wP)Cb, docetaxel (paclitaxel weekly) plus carboplatin; wP, paclitaxel weekly.

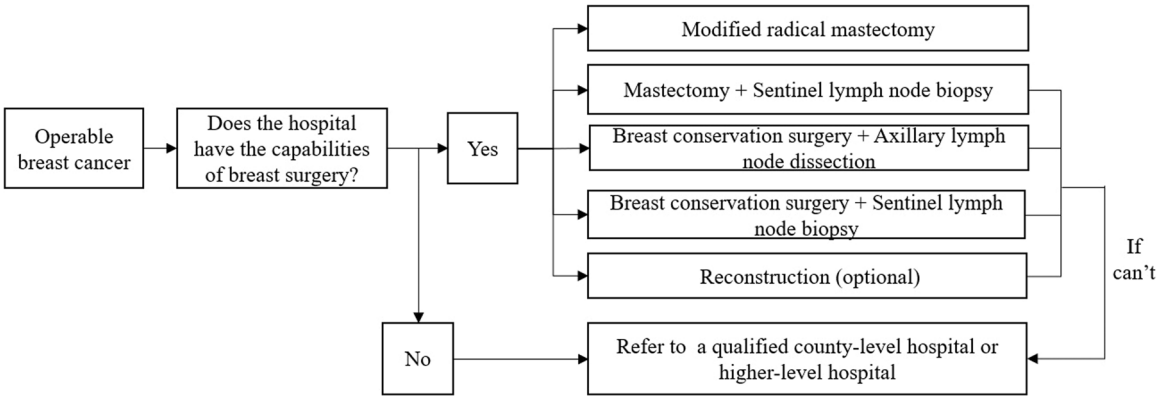

FIGURE 6 | County-level surgical treatment pathway for breast cancer [8, 10, 13].

information: tumor size, histological type, histological grade, presence or absence of combined DCIS, presence or absence of vascular and nerve invasion, presence or absence of tumor tissue in the nipple and margin, lymph node status, immunohistochemical markers such as ER, PR, HER2, and Ki-67. The advent of new antitumor drugs and the development of precision treatment concepts have heightened the requirements for pathological diagnosis, including the interpretation of HER2 low (IHC2+/ISH− or IHC1+) and the detection and interpretation of PD-L1.

County-level Guideline Recommendation 3: If county-level hospitals lack the necessary imaging equipment or interpretive expertise, or in instances of complex cases, patients should be referred to higher-level facilities or consulted remotely.

County-level Guideline Recommendation 4: Pathology departments in county-level hospitals are often underdeveloped. When necessary, tumor samples should be sent to superior hospital pathology departments or qualified third-party testing agencies. Alternatively, remote pathology consultations should be conducted to obtain accurate histopathological results and molecular characteristics (e.g., HER2 expression or amplification status) to guide treatment decisions.

County-level Guideline Recommendation 5: County-level hospitals should proactively organize and conduct multidisciplinary team (MDT) comprehensive diagnoses and treatments for breast cancer cases. This should include participation from (breast) surgery, medical oncology, radiation oncology, pathology, and imaging departments. MDT discussions should be completed in the county hospital, a superior hospital, or via remote consultation with a superior hospital before initiating the patient's treatment to ensure standardized and individualized breast cancer care.

4 | Treatment Pathways for County-Level Breast Cancer

A comprehensive treatment approach should be adopted for breast cancer, considering both the biological behavior of the tumor and the patient's physical condition. A combination of local and systemic therapies should be utilized to improve efficacy and patient quality of life. All drug recommendations in the treatment pathways are approved by the National Medical Products Administration of China for breast cancer treatment. Recommended regimens are prioritized based on the level of evidence, and local drug availability and affordability should be considered in treatment selection.

4.1 | Treatment Pathways for Early-Stage Breast Cancer

4.1.1 | Neoadjuvant Treatment for Breast Cancer

Neoadjuvant treatment, including neoadjuvant chemotherapy, targeted therapy, and endocrine therapy, involves systemic therapy as the initial component of antitumor treatment. The goals are to reduce the clinical stage of the tumor, increase resection and breast conservation rates, and gather drug sensitivity and prognostic information. Neoadjuvant therapy is considered for patients with the following conditions: (1) tumor size larger than 5 cm; (2) axillary lymph node metastases; (3) HER2-positive or triple-negative tumors generally larger than 2 cm; and (4) those desiring breast conservation but having relatively large tumors that complicate breast conservation efforts [12, 14, 17].

4.1.2 | Surgical Treatment

The surgical management of invasive breast cancer includes procedures targeting both the breast and axillary lymph nodes. Breast surgery options include mastectomy and breast-conserving surgery, with strict adherence to the indications for breast-conserving surgery. For patients who prefer breast conservation, find postoperative radiotherapy acceptable, and have tumors that can be completely resected with safe margins, breast-conserving surgery offers favorable cosmetic results. Patients opting for mastectomy can also achieve satisfactory cosmetic results through breast reconstruction, provided that reconstructive surgery does not delay or interfere with adjuvant therapy.

Evaluation of the axillary lymph node status is essential in cases of invasive breast cancer. Sentinel lymph node biopsy (SLNB) and axillary lymph node dissection are the primary surgical techniques employed. For clinically node-negative early-stage breast cancer patients, SLNB is recommended as the preferred approach for axillary management. Patients with a negative SLNB can avoid axillary lymph node dissection, thereby reducing the risk of complications such as upper limb edema. Conversely, patients with a positive SLNB should undergo supplementary axillary lymph node dissection, ensuring that a minimum of 10 axillary lymph nodes are dissected to accurately assess the axillary nodal status.

County-level Guideline Recommendation 6: County-level hospitals performing breast-conserving surgery must ensure their pathology departments are capable of margin assessment. If a patient qualifies for breast-conserving surgery but the hospital lacks the necessary conditions, referral to a same-level or superior hospital with the capability to perform the surgery is recommended. For hospitals with adequate pathology and surgical capabilities but lacking radiotherapy equipment and technology, postoperative referral to superior hospitals for radiotherapy is advised.

County-level Guideline Recommendation 7: Given the high technical requirements and the relative infrequency of breast reconstruction in county-level hospitals, patients opting for total mastectomy who desire breast reconstruction should be referred to qualified same-level or superior hospitals.

County-level Guideline Recommendation 8: SLNB necessitates tracer agents and coordination among surgery, imaging, and pathology departments. Hospitals without these technical capabilities should refer suitable SLNB patients to same-level or superior hospitals equipped to perform the procedure.

4.1.3 | Radiotherapy

In principle, all patients undergoing breast-conserving surgery should receive radiotherapy. For patients undergoing modified radical mastectomy, adjuvant radiotherapy is indicated if any of the following criteria are met: (1) Primary tumor stage T3–4; (2) Regional lymph node stage N2 or higher; and (3) For T1-2 and N1, postoperative radiotherapy may be considered. For patients not requiring adjuvant chemotherapy, radiotherapy should commence within 8 weeks post-surgery. For patients requiring adjuvant chemotherapy, radiotherapy should begin 4–8 weeks post-chemotherapy. Comprehensive records of radiotherapy, including technique, target definition, and dose, are essential for evaluating the standardization of breast cancer treatment, the potential for re-irradiation, and radiotherapy-related complications.

County-level Guideline Recommendation 9: Recognizing that some county-level hospitals may lack radiotherapy departments, establishing referral mechanisms with same-level or superior hospital radiotherapy departments in the region is recommended. This ensures that county-level hospital patients receive timely postoperative radiotherapy.

4.1.4 | Adjuvant Chemotherapy

Breast cancer patients with axillary lymph node metastasis typically require adjuvant chemotherapy. In cases of node-negative breast cancer, adjuvant chemotherapy should be considered if other high-

risk factors are present (e.g., age < 35 years, tumor size > 2 cm, Grade II–III, vascular invasion, HER2+, ER/PR− [Figure 7 for risk assessment]). The selection of chemotherapy regimens should be based on molecular subtypes in accordance with national guidelines (Figures 8 and 9). For patients with triple-negative and node-positive breast cancer, dose-dense chemotherapy is the preferred adjuvant therapy. For patients who have undergone neoadjuvant therapy, the adjuvant treatment regimen should be determined based on preoperative chemotherapy cycles, treatment efficacy, and postoperative pathology. Chemotherapy can impair ovarian function and reduce fertility. Therefore, fertility preservation should be considered at diagnosis and implemented before the initiation of systemic treatment for patients desiring fertility. Assisted reproductive technologies such as embryo freezing, oocyte freezing, immature oocyte freezing, and ovarian tissue freezing are available only in certain technologically advanced hospitals. Additionally, ovarian function protection with gonadotropin-releasing hormone analogs (GnRHa) should be considered during chemotherapy. GnRHa administration is recommended to start 2 weeks before chemotherapy, continue once every 4 weeks, and extend until 2 weeks after the completion of chemotherapy.

County-level Guideline Recommendation 10: It is recommended that primary hospitals refer patients undergoing assisted reproductive technology to reproductive centers at superior hospitals to implement relevant technologies as soon as possible, thereby avoiding delays in antitumor treatment.

4.1.5 | Adjunctive Targeted Therapy

Trastuzumab can be administered to patients with HER2-positive primary invasive foci greater than 0.5 cm. For patients at high risk of recurrence, such as those with lymph node positivity, the combination of trastuzumab and pertuzumab is recommended. Dual-target therapy may also be considered for

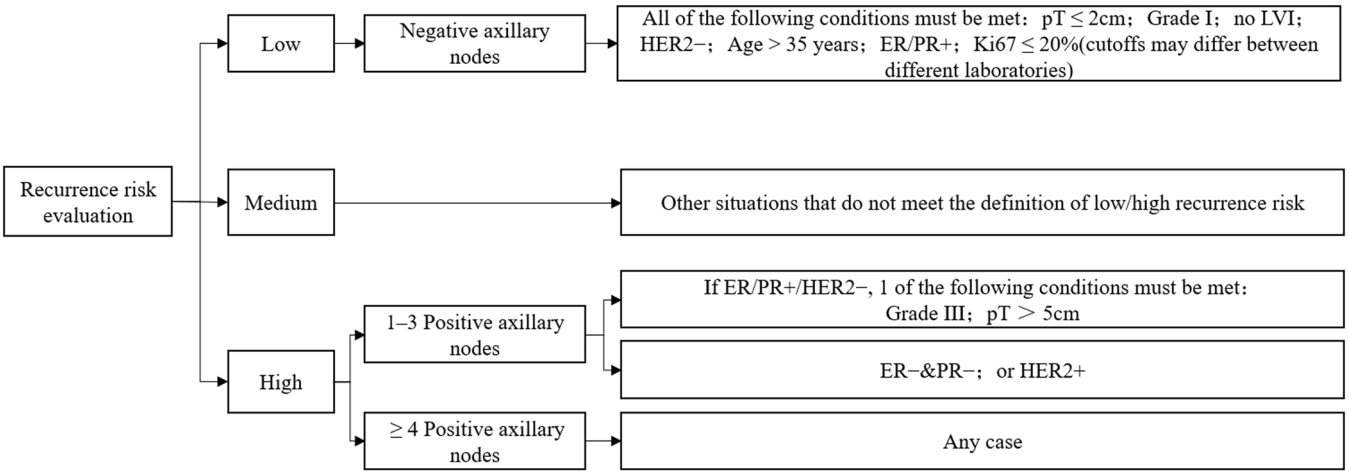

FIGURE 7 | County-level breast cancer recurrence risk assessment. ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; LVI, lymph vascular invasion; PR, progesterone receptor. There is currently a lack of original multi-gene testing products such as Oncotype DX in China. Most of them are third-party laboratories using self-made testing tools. Quality control of test results is difficult and expensive, so this guide does not include relevant recommendations.

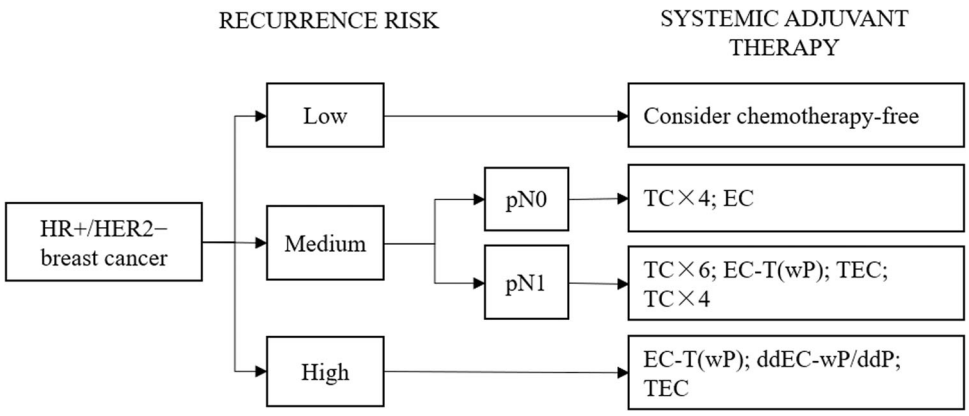

FIGURE 8 | Adjuvant chemotherapy pathway for HR+/HER2− breast cancer. ddEC, dose-dense epirubicin plus cyclophosphamide; ddP, dose-dense paclitaxel; EC, epirubicin plus cyclophosphamide; EC-T, epirubicin plus cyclophosphamide followed by docetaxel; HER2−, human epidermal growth factor receptor 2 negative; HR+, hormone receptor positive; TC, docetaxel plus cyclophosphamide; TEC, docetaxel plus epirubicin plus cyclophosphamide; wP, weekly paclitaxel.

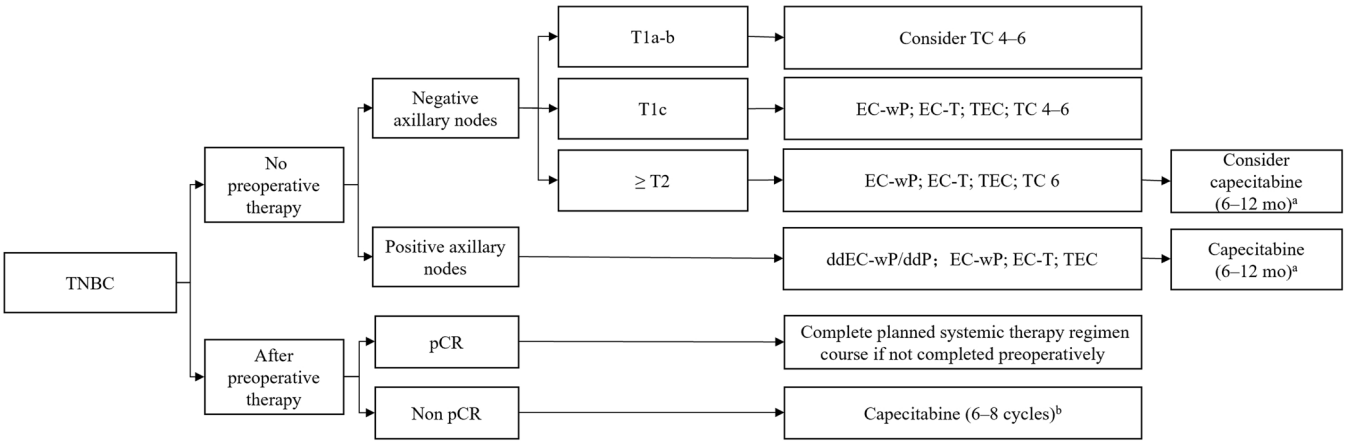

FIGURE 9 | Adjuvant chemotherapy pathway for triple-negative breast cancer. ddEC, dose-dense epirubicin plus cyclophosphamide administered on a bi-weekly intensive schedule; ddP, paclitaxel administered on a bi-weekly intensive schedule; EC, epirubicin plus cyclophosphamide; EC-T, Epirubicin plus cyclophosphamide followed by docetaxel; pCR, pathological complete response; TC, docetaxel plus cyclophosphamide; TEC, docetaxel plus epirubicin plus cyclophosphamide; wP, weekly paclitaxel. a—The recommended dose of capecitabine is 650 mg/m^2 PO twice daily for 1 year. b—The recommended dose of capecitabine is 1000–1250 mg/m^2 PO twice daily d1-14 q21d for 6 to 8 cycles.

lymph node-negative patients with adverse prognostic factors (e.g., ki67 > 30%, G3). Patients with a moderate to high risk of recurrence, particularly those with positive ER, may benefit from 1 year of intensive tyrosine kinase inhibitor therapy, such as neratinib, following the completion of trastuzumab therapy.

County-level Guideline Recommendation 11: Some county-level hospitals may lack access to drugs such as pertuzumab and neratinib. It is recommended to establish drug procurement channels for major diseases in collaboration with hospitals of the same or higher level within the region.

4.1.6 | Adjuvant Endocrine Therapy

In principle, patients with positive hormone receptor ER or positive PR should receive postoperative adjuvant endocrine therapy. An ER expression of 1%–10% is considered low. The biological behavior of low ER expression is generally similar to that of ER-negative breast cancer patients, and this should be taken into account during decision-making.

The assessment of ovarian function is crucial for selecting appropriate adjuvant endocrine therapy. Regardless of whether the patient undergoes chemotherapy, it is essential to evaluate the menstrual condition before systemic therapy. Six hormone levels should be measured to determine the patient's ovarian function status, facilitating the development of a comprehensive adjuvant treatment plan. It is important to note that a patient who was not menopausal before chemotherapy cannot be considered postmenopausal solely based on the cessation of menstruation following chemotherapy.

The definition of menopause: Menopause refers to the permanent cessation of menstruation, indicating a persistent reduction in estrogen synthesis by the ovaries. A patient is considered to have menopausal status if they meet any of the following criteria: (1) bilateral ovariectomy; (2) age 60 years or older; (3) age under 60 years, with natural menopause for 12 months, FSH and estradiol levels within the postmenopausal range without chemotherapy, tamoxifen, toremifene, or ovarian castration in the past year; (4) patients under 60 years taking tamoxifen or toremifene must have serial FSH and estradiol levels within the postmenopausal range.

4.2 | Treatment Pathways for Advanced Breast Cancer

Advanced (Stage IV) breast cancer requires a comprehensive treatment approach, primarily utilizing systemic therapy, with the addition of local therapy as appropriate. Systemic therapy should be prioritized as the initial antitumor intervention. The formulation of the treatment plan should be individualized, guided by evidence-based medicine, and take into account the local economic context, drug availability, and patient-specific factors. Throughout the treatment process, the involvement of patients' families in discussions is encouraged, multidisciplinary consultations are recommended, and participation in well-designed and high-quality clinical trials is advocated when feasible. For county-level hospitals lacking the capability to diagnose and treat advanced breast cancer, it is advisable to transfer patients to higher-level medical facilities.

Before treatment, a thorough evaluation of patient-specific factors is essential, including general health status, staging, previous treatment (curative effect, adverse reactions, and tolerance), disease-free interval, tumor burden (site and number of metastases), menstrual status, comorbidities, and the treatment preferences of both the patient and their family. It is crucial to clarify the pathological diagnosis and supplement it with breast cancer genotyping and relevant genetic testing. The pathological diagnosis of Stage IV breast cancer must be definitive, and for recurrent or metastatic breast cancer posttreatment, re-evaluation of the pathological diagnosis is recommended.

Determination of baseline status before the initiation of treatment for advanced breast cancer is imperative. Follow-up treatment efficacy should be assessed using the Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST 1.1). Effective clinical treatment modalities for patients with advanced breast cancer include chemotherapy, endocrine therapy, targeted therapy, immunotherapy, local therapy (e.g., palliative surgery, radiotherapy, interventional procedures), and traditional Chinese medicine. Indications for preferential chemotherapy include ER and PR negative status, HER2-positive status, shorter disease-free survival (< 2 years), rapid tumor progression with pronounced symptoms, and extensive visceral metastases. Patients with HER2-positive are more likely to benefit from anti-HER2 therapy, while those with ER and/or PR positive are more likely to benefit from endocrine therapy.

County-level Guideline Recommendation 12: In the diagnosis and treatment of advanced (Stage IV) breast cancer, county-level hospitals should comprehensively evaluate the general condition of patients, confirm the current pathological diagnosis, molecular classification, and TNM staging, and formulate a comprehensive antitumor treatment plan. It is recommended to conduct multidisciplinary consultations or jointly formulate antitumor treatment plans with superior hospitals. Qualified patients are encouraged to participate in clinical trials.

County-level Guideline Recommendation 13: County-level hospitals should perform a comprehensive imaging examination before the initial systemic treatment of advanced (Stage IV) breast cancer, and it is recommended to use the same imaging evaluation method for subsequent assessments. For patients with new metastases, a repeat biopsy is recommended to elucidate the pathological characteristics.

4.2.1 | HER2-Positive Advanced Breast Cancer Treatment

Patients with HER2-positive advanced breast cancer should initiate anti-HER2 therapy as soon as possible unless contraindicated. For patients with recurrent and metastatic breast cancer, re-biopsy or the latest pathological examination and immunohistochemical results should guide clinical treatment. If feasible, a repeat biopsy of the metastases should be performed to clarify the HER2 status of the metastases. When there is a discrepancy between the HER2 status of primary and metastatic sites, anti-HER2 treatment should be recommended if either site tests positive (Figures 10–12).

The treatment pathway for HER2-positive advanced breast cancer patients is as follows.

For HER2-positive advanced breast cancer, first-line antitumor therapy (Figure 13) should typically include chemotherapy for a minimum of 6–8 cycles, contingent upon patient efficacy and tolerance. The optimal duration for anti-HER2 therapy remains unclear; however, it can be continued in the absence of disease progression or intolerable adverse effects. In the context of second-line and subsequent antitumor treatments for HER2-positive advanced breast cancer, the treatment regimen should be tailored according to previous therapies (Figure 14). Clinical attention is crucial for patients with low HER2 expression, as clinical research data, including findings from the DESTINY-Breast04 trial, indicate that patients with low HER2 expression may benefit from novel ADC drug treatments (Figures 15–23).

For patients with HR+/HER2+ advanced breast cancer, if chemotherapy is tolerated, a combination of anti-HER2 therapy and chemotherapy is recommended. In cases where chemotherapy is not suitable, or progression is slow, a combination of anti-HER2 therapy (preferably dual-targeted therapy) and endocrine therapy is advisable. Combination therapy has been shown to prolong PFS compared with endocrine therapy alone. If first-line chemotherapy combined with anti-HER2 therapy is beneficial and the disease remains stable, maintenance therapy with endocrine and anti-HER2 therapy may be considered despite the absence of randomized trial data supporting this regimen. Participation in clinical trials is recommended for eligible patients.

4.2.2 | Endocrine Therapy

HR+/HER2− breast cancer represents the most common clinical subtype among breast cancer patients and can be effectively managed with endocrine therapy. Endocrine therapy is an important approach for treating hormone receptor-positive

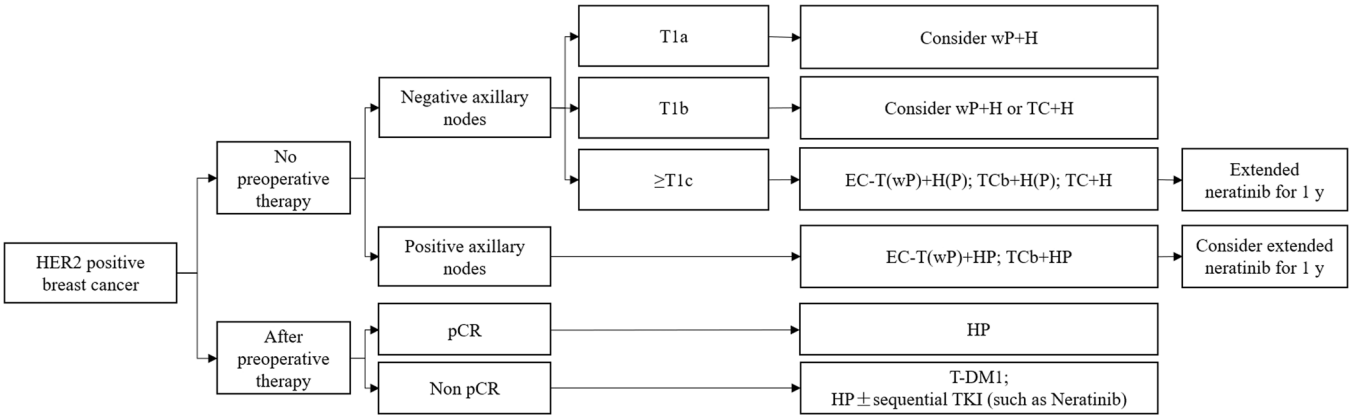

FIGURE 10 | Adjuvant therapy pathway for HER2+ breast cancer. EC-T, epirubicin plus cyclophosphamide followed by docetaxel; HER2, human epidermal growth factor receptor 2; H, trastuzumab; pCR, pathological complete response; wP, weekly paclitaxel; TC, docetaxel plus cyclophosphamide; TCb, Docetaxel plus carboplatin; P, pertuzumab; TKI, tyrosine kinase inhibitor.

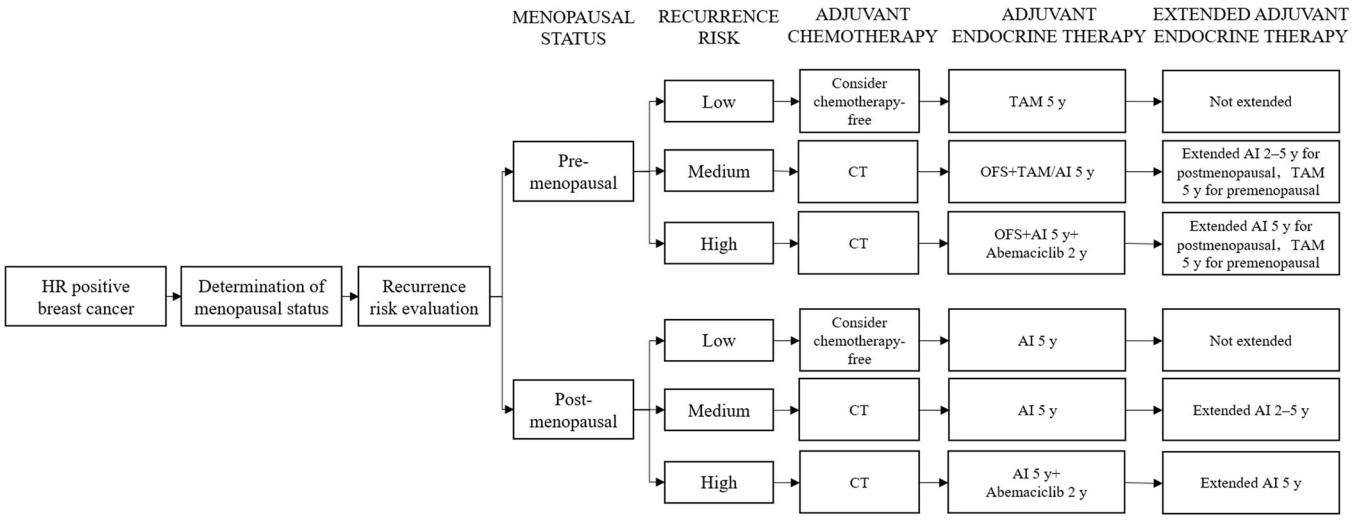

FIGURE 11 | Adjuvant therapy pathway for hormone receptor-positive breast cancer. AI, aromatase inhibitor; CT, chemotherapy; OFS, ovarian function suppression; TAM, tamoxifen.

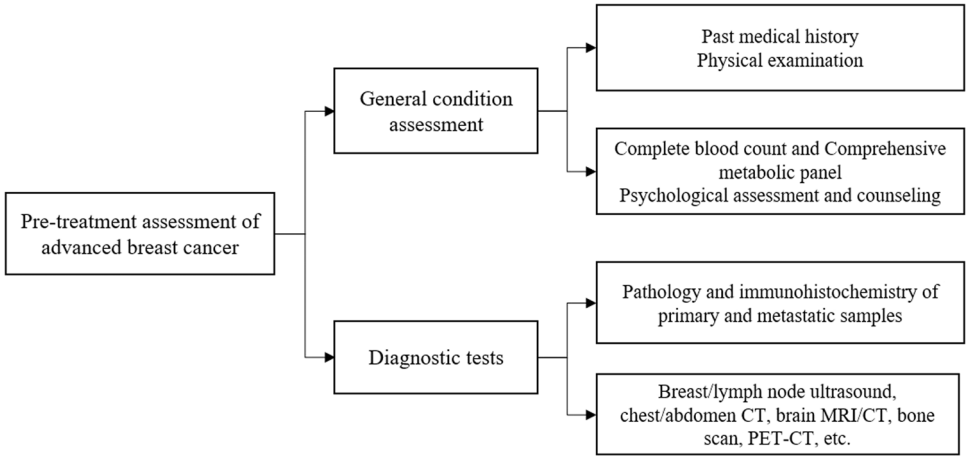

FIGURE 12 | Pretreatment assessment for advanced breast cancer. PET-CT, positron emission tomography-computed tomography.

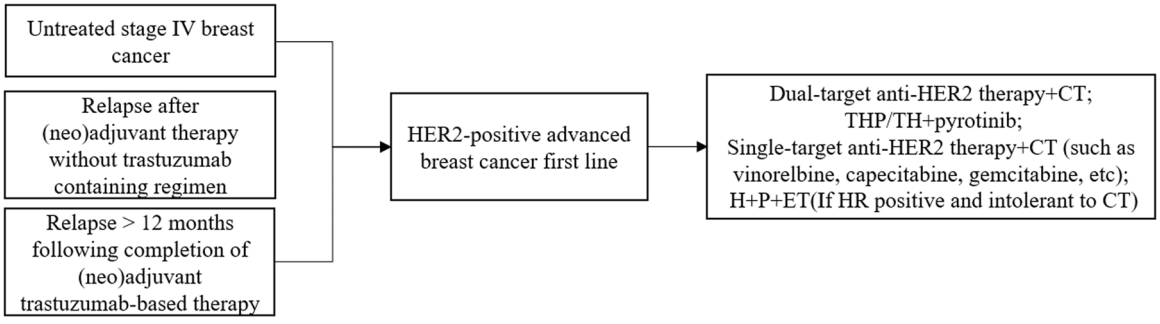

FIGURE 13 | First-line treatment for HER2-positive advanced breast cancer. H, trastuzumab; HER2, human epidermal growth factor receptor 2; P, pertuzumab; TH, taxane plus trastuzumab; THP, taxane plus trastuzumab plus pertuzumab.

advanced breast cancer, and the combination of targeted therapy with endocrine therapy has become the standard treatment for patients with HR+/HER2− advanced breast cancer.

Following a systematic evaluation, postmenopausal patients with HR+ advanced breast cancer should receive antitumor treatment based on the following pathway.

Premenopausal patients with HR+ advanced breast cancer should undergo surgical or medical castration followed by endocrine therapy as administered to postmenopausal patients. For HR+/HER2− advanced breast cancer, endocrine therapy remains the preferred treatment option, even in the presence of visceral metastasis, unless a visceral crisis is present. A visceral crisis is characterized by severe organ dysfunction as evidenced by

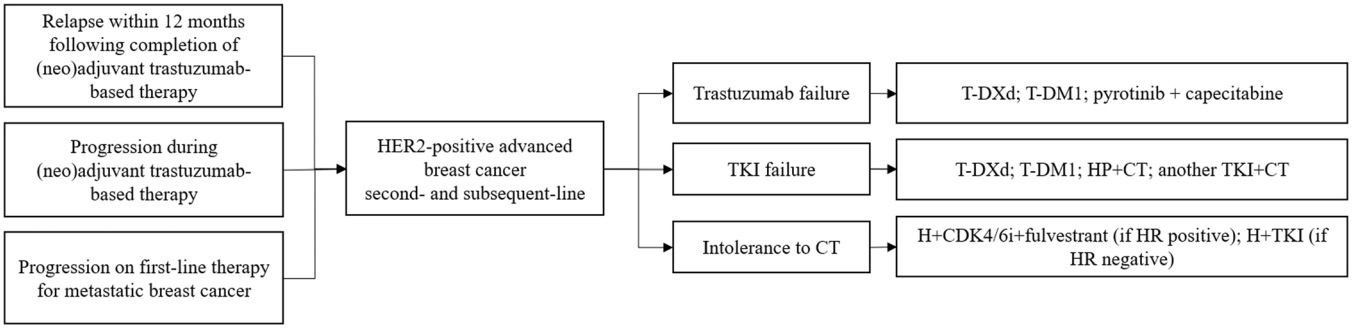

FIGURE 14 | Second- and subsequent-line treatment for HER2-positive advanced breast cancer. CDK4/6i, CDK4/6 inhibitors; H, trastuzumab; HER2, human epidermal growth factor receptor 2; HP, trastuzumab plus pertuzumab; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan; TKI, tyrosine kinase inhibitor.

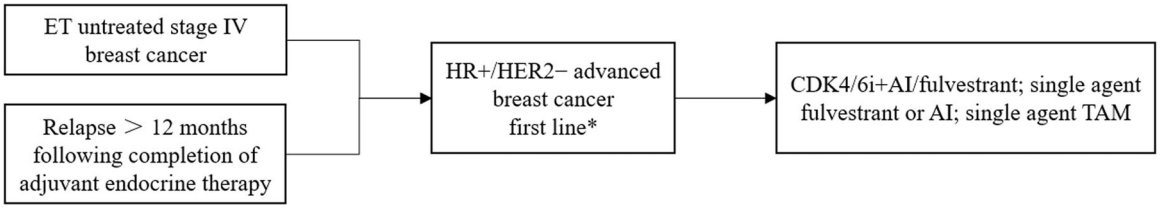

FIGURE 15 | First-line treatment for HR+/HER2− advanced breast cancer. AI, aromatase inhibitors; CDK4/6i, CDK4/6 inhibitors; HER2−, human epidermal growth factor receptor 2 negative; HR+, hormone receptor positive; TAM, tamoxifen. *Strictly definition of first-line targets refers to patients diagnosed with de novo stage IV breast cancer or relapsed endocrine-sensitive breast cancer. If relapsing more than 1 year following completion of adjuvant endocrine therapy, adjuvant endocrine drugs can theoretically still be used in the first-line setting. However, in actual clinical operations, unused drugs are preferred.

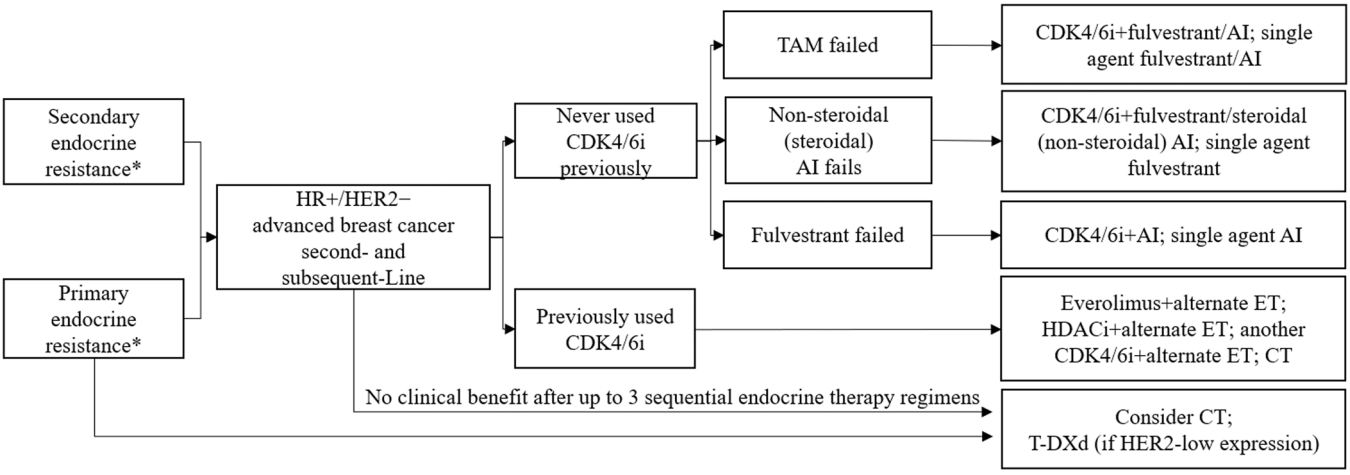

FIGURE 16 | Second- and subsequent-line treatment for HR+/HER2− advanced breast cancer. AI, aromatase inhibitors; CDK4/6i, CDK4/6 inhibitors; ET, endocrine therapy; HDACi, histone deacetylase inhibitors; HER2−, human epidermal growth factor receptor 2 negative; HR+, hormone receptor positive; TAM, tamoxifen; T-DXd, trastuzumab deruxtecan. *Primary endocrine resistance is defined as a relapse while on the first 2 years of adjuvant endocrine therapy, or progression within 6 months of first-line endocrine therapy. *Secondary endocrine resistance is defined as a relapse while on adjuvant endocrine therapy but after the first 2 years or a relapse within 12 months of completing adjuvant endocrine therapy or progression while on ≥ 6 months of first-line endocrine therapy.

symptoms, signs, laboratory tests, and rapid disease progression. It denotes critical organ damage necessitating immediate and effective treatment to control disease progression, particularly when further treatment opportunities may be lost upon progression. The following conditions constitute a visceral crisis: (1) lung cancerous lymphangitis requiring oxygen at rest; (2) dyspnea that worsens at rest and is unrelieved by pleural effusion drainage; (3) diffuse liver metastasis with bilirubin levels ≥ 1.5 times the upper limit of normal (without biliary obstruction); (4) extensive bone marrow metastasis; (5) meningeal metastasis; and (6) symptomatic brain parenchymal metastasis.

For second-line endocrine therapy in patients with HR+ advanced breast cancer, the choice of medications should consider previous endocrine treatments and responses. Drugs previously used and proven resistant should be avoided. If a CDK4/6

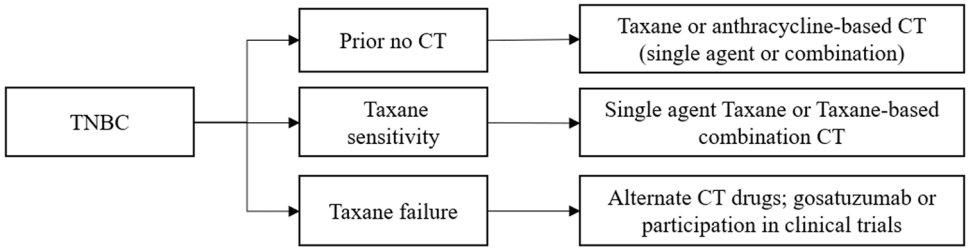

FIGURE 17 | Advanced triple-negative breast cancer treatment pathway. CT, chemotherapy; TNBC, triple-negative breast cancer.

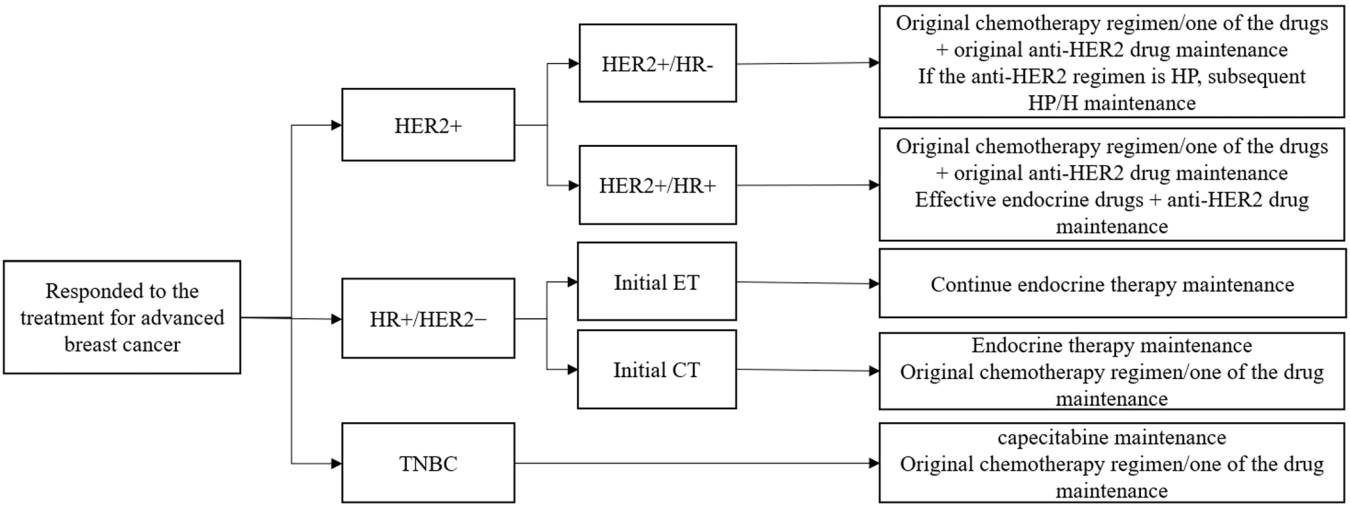

FIGURE 18 | Advanced breast cancer maintenance therapy pathway. CT, chemotherapy; ET, endocrine therapy; H, Trastuzumab; HER2, human epidermal growth factor receptor 2; HP, trastuzumab plus pertuzumab; HR, hormone receptor; TNBC, triple-negative breast cancer.

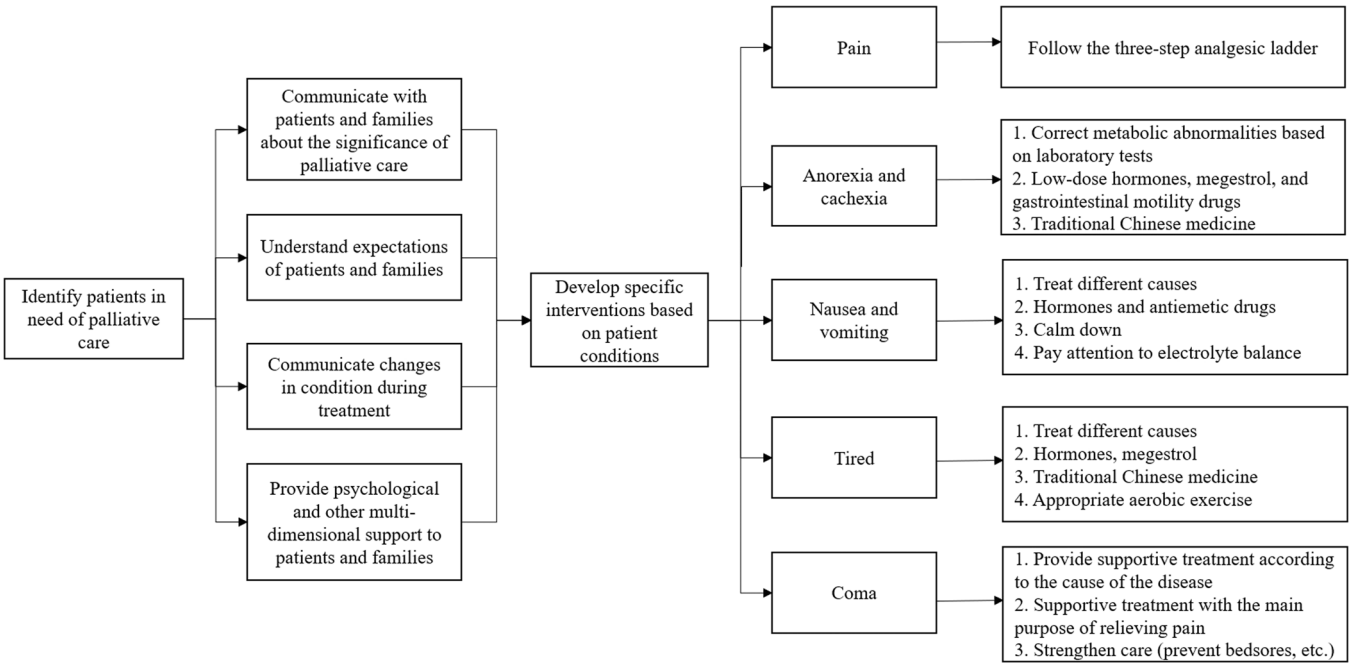

FIGURE 19 | Palliative care management pathway for end-stage breast cancer.

inhibitor was not utilized in prior treatment, its combination with endocrine therapy is preferred.

County-level Guideline Recommendation 14: For the diagnosis and treatment of late-stage (IV) HR+ breast cancer in county-level hospitals, targeted therapy combined with endocrine therapy is the standard treatment for HR+/HER2− breast cancer. In cases of visceral crisis, systemic chemotherapy may be initiated, followed by endocrine maintenance therapy. Premenopausal patients undergoing OFS should follow the treatment pathway for postmenopausal HR+ advanced breast cancer.

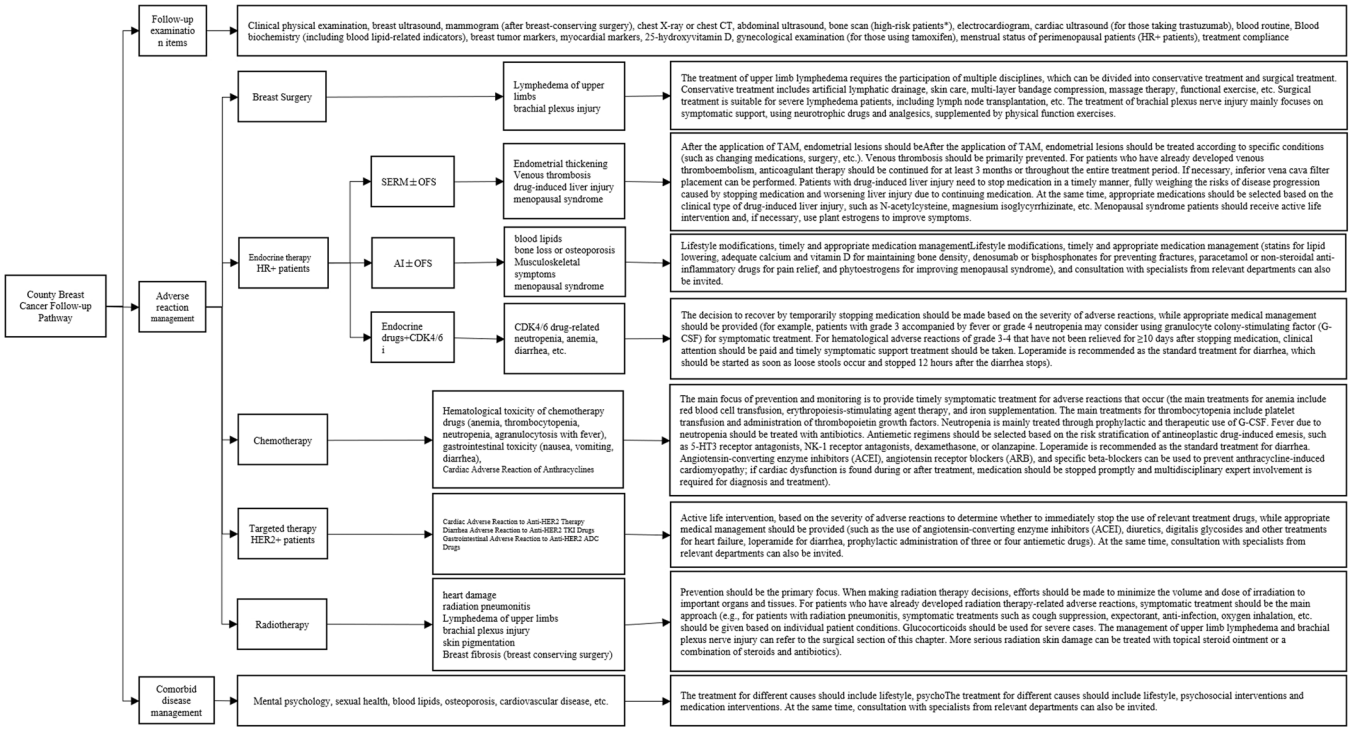

FIGURE 20 | County-level breast cancer follow-up pathway. ADC, antibody-drug conjugate; AI, aromatase inhibitor; CDK4/6i, CDK4/6 inhibitor; HER2, human epidermal growth factor receptor 2; HR, hormone receptor; SERM, selective estrogen receptor modulator; OFS, ovarian function suppression; TKI, tyrosine kinase inhibitor. *It is suggested that patients with high-risk factors, such as axillary lymph node metastasis > 4, should undergo regular bone scan examinations.

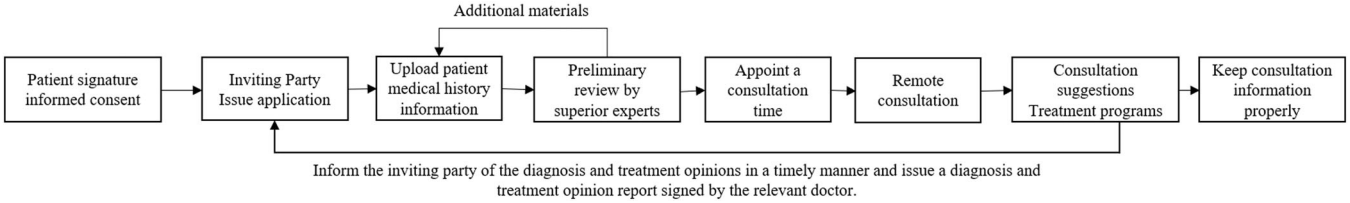

FIGURE 21 | County-level smart medical remote consultation pathway for breast cancer.

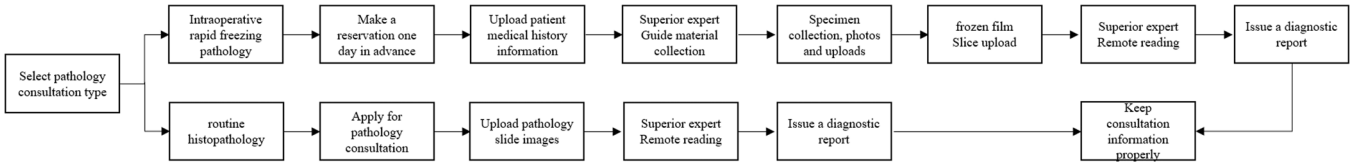

FIGURE 22 | County-level smart medical remote pathology pathway for breast cancer.

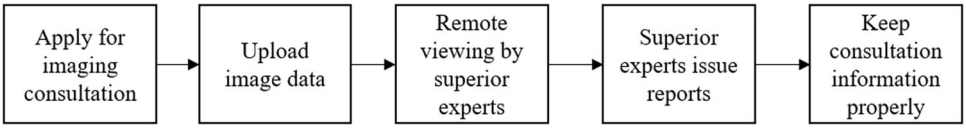

FIGURE 23 | County-level smart medical remote imaging pathway for breast cancer.

4.2.3 | Treatment of Patients With Advanced Triple-Negative Breast Cancer

Triple-negative breast cancer (TNBC) is characterized by the absence of estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2). Conventional endocrine and HER2-targeted therapies are ineffective for TNBC, which is prone to visceral metastasis and has a poor prognosis. The primary treatment options for advanced TNBC include chemotherapy with agents such as paclitaxel, capecitabine, gemcitabine, platinum, eribulin, and utideron, as well as combination regimens like GT and GP. In recent years, immunotherapy, targeted therapy, and new ADC drugs are changing the clinical management of TNBC, although significant challenges remain.

Following a systematic evaluation of advanced triple-negative breast cancer, antitumor treatment should be administered based on the outlined clinical pathways.

Taxane treatment failure is defined as disease progression during taxane rescue therapy (after the completion of at least two cycles) or by recurrence and metastasis within 12 months following the conclusion of adjuvant therapy.

County-level Guideline Recommendation 15: In the management of patients with advanced triple-negative breast cancer, county-level hospitals prefer the use of taxane-based monotherapy or combination chemotherapy. Upon failure of taxane treatment, alternative pharmacologic agents should be considered. Re-biopsy is recommended following the progression of advanced triple-negative breast cancer to enhance the array of treatment options available to patients. Individuals exhibiting low HER2 expression may derive benefit from treatment with T-DXd, a novel ADC. Participation in clinical trials is strongly encouraged where feasible. For drugs not yet marketed or approved for relevant indications in China, clinical practice requires judicious selection.

4.2.4 | Maintenance Treatment for Patients With Advanced Breast Cancer

Maintenance therapy is generally defined as the continuation of treatment in patients with advanced breast cancer who have achieved disease control following standardized first-line chemotherapy (typically 6–8 weeks). This prolonged therapy aims to control tumor progression, alleviate symptoms, improve quality of life, and extend PFS. Presently, maintenance therapy is not restricted to first-line treatment alone. It is recommended that patients with advanced breast cancer undergo maintenance therapy following standard and effective treatment regimens. Maintenance therapy methods include chemotherapy, targeted therapy, and endocrine therapy. This approach is unanimously endorsed by major guidelines [14, 17, 18]. After effective treatment, maintenance therapy should be administered to patients with advanced breast cancer according to the following pathway.

County-level Guideline Recommendation 16: In the diagnosis and treatment of advanced breast cancer, county-level hospitals should adhere to established standards and provide follow-up maintenance treatment tailored to the patient's specific condition. Endocrine or targeted therapy should be prioritized for maintenance therapy, with capecitabine monotherapy recommended for patients who respond to chemotherapy. The original regimen or an alternative drug may also be used as maintenance treatment.

4.2.5 | Management Pathway of Palliative Care for End-Stage Breast Cancer

Palliative care for end-stage breast cancer emphasizes the identification, assessment, control, and treatment of both physical and psychological suffering, as well as the threats to patients' quality of life. When formulating a treatment plan, it is essential to identify and assess the population receiving palliative care, considering factors such as the patient's disease status, preferences, family circumstances, and economic situation. Drug interventions should be tailored to the underlying causes of the disease.

Before initiating palliative treatment for end-stage breast cancer, it is essential to clarify the treatment wishes and expectations of patients and their families and to formulate a comprehensive palliative treatment plan. The primary objective of palliative care for patients with end-stage breast cancer is to manage symptoms, such as pain, that significantly impact the patient's quality of life. Symptom management involves identifying the underlying causes and implementing appropriate interventions. Concurrently, palliative support is enhanced based on laboratory test results to further improve patients' quality of life.

County-level Guideline Recommendation 17: County-level hospitals providing palliative care for patients with end-stage breast cancer should conduct a thorough assessment of the patient's overall condition, identify the cause of symptoms, and offer appropriate supportive care. Given potential challenges in diagnosis and treatment, it is recommended that county-level hospitals engage in comprehensive consultations with hospitals of the same or higher level within the region.

5 | Follow-Up Pathway for Breast Cancer at the County Level

It is recommended to refer to the *Comprehensive Management Guideline for Breast Cancer Follow-up and Healthcare (2022 Edition)* [19].

The objectives of follow-up include the following: (1) Early detection of local recurrences, metastatic disease, and second primary tumors. (2) Evaluation and treatment of therapy-related complications and associated comorbidities. (3) Provision of psychological support and information to facilitate a return to normal life after breast cancer treatment.

Long-term follow-up for patients with early-stage breast cancer is crucial for the early detection of disease recurrence, metastasis, second primary tumors, treatment-related complications, and related comorbidities. Additionally, it provides standardized guidance to promote recovery.

Following the completion of breast cancer therapy, ongoing long-term follow-up is necessary to monitor for disease recurrence. During the treatment of advanced breast cancer, regular evaluation of tumor response is required to guide the selection of antitumor regimens. Elevated tumor markers alone should not be used as the sole basis for altering treatment regimens; instead, a combination of symptoms, signs, and imaging examinations should be used to determine the need for changes in the treatment plan.

Recommended follow-up items and frequency: Clinical examination: once every 4–6 months for the first 2 years, once every 6 months from years 3 to 5, and annually thereafter. Breast ultrasound: once every 6 months. Mammography: once a year. Chest CT: once a year, county-level hospitals without CT equipment should refer patients to higher-level hospitals for follow-up. Abdominal ultrasound: once every 6 months, annually after 3 years. Patients with high-risk factors, such as more than 4

axillary lymph node metastases, should undergo baseline bone scintigraphy and whole-body bone scintigraphy once a year, then once every 2 years after 5 years. Blood routine, blood biochemistry, and breast cancer markers: measured every 6 months and annually after 3 years. Patients receiving tamoxifen should have an annual pelvic examination [14, 19–24].

County-level Guideline Recommendation 18: Follow-up and reexamination of early breast cancer should be completed in county-level hospitals, preferably at the hospital where the patient previously received antitumor treatment. For patients with stable disease, community hospitals or township health centers should be contacted simultaneously to include these patients in the chronic disease management list. Daily monitoring, rehabilitation guidance, and reminders for regular follow-up should be provided. If local recurrence or distant metastatic breast cancer is suspected, patients should be transferred to a qualified county hospital or higher-level hospital for evaluation and treatment planning. During follow-up of advanced breast cancer, serial imaging evaluations at the same hospital are recommended to ensure result accuracy.

County-level Guideline Recommendation 19: Given the possible inconvenience of transportation for county-level patients, it is recommended to closely monitor changes in patients' physical conditions through online follow-up, such as telephone consultations, during intervals between hospital visits.

6 | Smart Medical Care for Breast Cancer at the County Level

As an intermediate link in hierarchical diagnosis and treatment, county-level hospitals should leverage information technology to promote bidirectional referral and follow-up. These hospitals should serve as a bridge between higher- and lower-level hospitals, facilitating the sharing of medical resources and patient management.

County-level hospitals are encouraged to establish remote consultation systems and collaborate with provincial and municipal hospitals. Services provided should include remote consultation, remote electrocardiography diagnosis, remote medical imaging diagnosis, and remote pathology diagnosis [25]. These efforts should optimize the intelligent medical diagnosis and treatment pathways for breast cancer in counties in accordance with the *Remote Medical Service Management Standards (Trial)* and *Internet Diagnosis and Treatment Management Measures (Trial)* issued by the National Health Commission [26].

Within the medical consortium or community, a stable mechanism for remote consultation, remote pathology diagnosis, and remote imaging diagnosis should be established to strengthen the technical support provided by higher-level hospitals to primary medical institutions.

6.1 | Remote Consultation

The inviting party (the hospital initiating the remote consultation) should organize remote medical services according to the patient's condition and wishes. The patient should be informed about the content and cost of remote medical services, and their written consent should be obtained by signing the informed consent form.

If the inviting party needs to discuss individual cases with the invited party (the higher-level hospital) through the remote medical service, an invitation should be sent directly or through a third-party platform. The invitation should include the reason, purpose, schedule, summary of medical records, and the professional and technical qualifications of the physician to be invited.

The invitee should responsibly arrange medical staff with the corresponding qualifications and technical capabilities to provide remote medical services in accordance with relevant laws, regulations, and clinical guidelines. The invitee should promptly notify the inviting party of their diagnosis and treatment opinions and issue a medical report signed by the relevant physicians. The inviting party should decide on the diagnosis and treatment plan based on the patient's clinical information and the invitee's opinions.

6.2 | Remote Pathology

The remote pathology platform enables pathologists to provide guidance on sampling, staining, slide preparation, diagnosis, and other related procedures. This support aims to enhance the skills of local physicians and mitigate the risk of treatment errors resulting from inaccurate pathological diagnoses.

Applications for remote pathology consultations should be submitted through provincial, municipal, or hospital-level online pathology platforms. For intraoperative rapid frozen pathology, applications must be submitted to a higher-level hospital at least 1 day in advance, along with the patient's medical history. For bilateral organs or specific sites, it is imperative to indicate the left and right sides or other surgical sampling locations. After the operation, images of the samples and frozen sections should be uploaded, after which superior pathologists will review the films and issue a report.

6.3 | Remote Imaging

County-level hospitals lacking the capability to interpret complex images can apply for remote image consultations with higher-level hospitals. This facilitates the decentralization of high-quality medical resources. The process is as follows.

6.4 | Intelligent Patient Management

Meta-analyses indicate that active psychological interventions and reminder interventions in breast cancer patients, particularly those undergoing early-stage endocrine adjuvant therapy, can significantly enhance patient compliance [27]. Compliance, in turn, is often positively correlated with the efficacy of the treatment [27, 28].

County-level hospitals are integral to patient management across county, township, and village levels. Effective management of breast cancer spans all treatment cycles and extends throughout the patient's survival period.

It is recommended that county-level hospitals establish chemotherapy day wards and infusion centers to enhance patient treatment convenience. Utilizing mobile smart devices, such as smartphones, can remind patients to adhere to review schedules, take medication punctually, self-monitor adverse reactions, and report these actively. Additionally, online patient education and remote follow-ups should be implemented. Adopting intelligent and convenient patient management strategies will contribute to achieving high-quality, long-term survival outcomes for patients at the county level.

Author Contributions

Bo Lan: project administration (lead), writing – original draft (lead), writing – review and editing (lead). **Ping Lu:** project administration (supporting), writing – original draft (supporting). **Mengyou Liu:** project administration (supporting), writing – original draft (supporting). **Fei Ma:** conceptualization (equal), resources (equal), writing – review and editing (equal).

Acknowledgments

Honorary Steering Commissioner:

Binghe Xu (Department of Clinical Trial Center, National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College).

Expert Committee:

Authors:

Bo Lan (Department of Medical Oncology, National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College), Ping Lu (Department of Medical Oncology, The First Affiliated Hospital of Xinxiang Medical University), Mengyou Liu (Department of Thyroid and Breast Surgery, Lixin County People's Hospital), Fei Ma (Department of Medical Oncology, National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College).

Steering Committee (in alphabetical order of last name):

Hui Li (Breast Surgery, Sichuan Cancer Hospital), Dequan Liu (Department of Breast Surgery, Yunnan Cancer Hospital, The Third Affiliated Hospital of Kunming Medical University), Jian Liu (Department of Medical Oncology, Fujian Provincial Cancer Hospital), Xinlan Liu (Department of Oncology, General Hospital of Ningxia Medical University), Yunjiang Liu (Department of Breast Center, Fourth Hospital of Hebei Medical University), Zhenzhen Liu (Department of Breast Disease, Henan Breast Cancer Center, The Affiliated Cancer Hospital of Zhengzhou University & Henan Cancer Hospital), Binlin Ma (Department of Breast and Thyroid Surgery, Cancer Hospital Affiliated to Xinjiang Medical University), Fei Ma (Department of Medical Oncology, National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College), Qinguo Mo (Breast Surgery, Guangxi Medical University Affiliated Tumor Hospital), Quchang Ouyang (Department of Medical Oncology, Hunan Cancer Hospital), Yueyin Pan (Oncology Chemotherapy Department, The First Affiliated Hospital of University of Science and Technology of China [Anhui Provincial Hospital]), Zhangjun Song (Department of Surgical Oncology, Shaanxi Provincial People's Hospital), Zhengkui Sun (Department of Breast Oncology Surgery, Jiangxi Cancer Hospital [The Second People's Hospital of Jiangxi Province]), Yuee Teng (Department of Medical Oncology, The First Hospital of China Medical University), Shusen Wang (Internal Medicine Oncology, Sun Yat-Sen University Cancer Center), Xiaojia Wang (Department of Breast Medical Oncology, Cancer Hospital of the University of Chinese Academy of Sciences [Zhejiang Cancer Hospital]), Yongsheng Wang (Department of Breast, Shandong Cancer Hospital), Xinhong Wu (Department of Breast Oncology, Hubei Cancer Hospital), Jin Zhang (The Third Department of Breast Cancer, Tianjin Medical University Cancer Institute and Hospital), Lili Zhang (Department of Oncology, Jiangsu Cancer Hospital), Qingyuan Zhang (Department of Medical Oncology, Harbin Medical University Cancer Hospital).

Writing Committee (in alphabetical order of last name):

Wenbo He (Department of Thyroid and Breast Surgery, Dingzhou City People's Hospital), Qiao Li (Department of Medical Oncology, National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College), Guoxiang Luo (Department of Thyroid and Breast Surgery, Xiantao First People's Hospital Affiliated To Yangtze University), Jun Luo (Department of Breast Surgery, Fengcheng People's Hospital), Qiuli Meng (Department of Oncology and Hematology, Gongyi City People's Hospital [Gongyi City General Hospital]), Qiong Qin (Department of Oncology, Dalate Banner People's Hospital), Honglan Qu (Department of Hematological Oncology, Inner Mongolia Forestry General Hospital), Yun Ren (Department of Surgical Oncology, Taihe County People's Hospital), Xiang Tan (Oncology Department, Anyue County People's Hospital), Huali Tang (Department of Oncology, Central Hospital of Zhuanghe City), Juan Wang (Department of Breast Surgery, The Third People's Hospital of Honghe Prefecture), Yanli Wang (Department of Oncology, Baoding NO.2 Central Hospital), Qianfu Wu (General Surgery Department, Guiping People's Hospital), Jing Yan (Department of Oncology, Dingyuan General Hospital), Feidu Zhou (Department of Breast and Thyroid Surgery, Liuyang People's Hospital).

Ethics Statement

The authors have nothing to report.

Consent

The authors have nothing to report.

Conflicts of Interest

Professor Fei Ma and Professor Binghe Xu are the members of the *Cancer Innovation* Editorial Board. To minimize bias, they were excluded from all editorial decision-making related to the acceptance of this article for publication. The remaining authors declare no conflicts of interest.

Data Availability Statement

The authors have nothing to report.

References

1. R. S. Zheng, S. W. Zhang, K. X. Sun, et al., "Cancer Statistics in China, 2016 (in Chinese)," *Chinese Journal of Oncology* 45, no. 3 (2023): 212–220, https://doi.org/10.3760/cma.j.cn112152-20220922-00647.

2. National Health Commission Expert Committee on Rational Use of Medicine, *Guideline For Rational Medication of Breast Cancer* (People's Health Publishing House, 2019).

3. National Cancer Center & National Oncology Quality Control Center, Guidelines for *Breast Cancer Screening and Early Diagnosis and Treatment in China* (People's Health Publishing House, 2019).

4. Breast Cancer Expert Committee of National Cancer Quality Control Center, "Quality Control Index for Standardized Diagnosis and Treatment of Breast Cancer in China (2022 Edition) (in Chinese)," *China Journal of Oncology* 44, no. 3 (2022): 203–208, https://doi.org/10.3760/cma.j.cn112152-20220104-00008.

5. General Office of the National Health Commission of the People's Republic of China, "Circular of the General Office of the National Health Commission on the Issuance of the 'Thousand Counties Project' Work Plan to Improve Comprehensive Capabilities of County-Level Hospitals [EB/OL], (2021–2025) (in Chinese)," accessed November 17, 2023, https://www.gov.cn/zhengce/zhengceku/2021-11/04/content_5648771.htm.

6. General Office of the National Health Commission of the People's Republic of China, "Professional Quality Control Indicators for Oncology (2023 Edition) (in Chinese) [EB/OL]," accessed March 27, 2023, http://www.nhc.gov.cn/yzygj/s7657/202303/d61a0abf132f4aaf9ebbb6d094764ad2.shtml.

7. State Council Office of the People's Republic of China, "Circular of the General Office of the State Council on the Issuance of the Outline of the National Healthcare Service System Plan (2015–2020) (in Chinese) [EB/OL]," accessed November 17, 2023, https://www.gov.cn/zhengce/content/2015-03/30/content_9560.htm?ivk_sa=1024320u.

8. State Council Office of the People's Republic of China, "Opinions of the General Office of the State Council on the Implementation of Comprehensive Reform of County-Level Public Hospitals in a Comprehensive Way (in Chinese) [EB/OL]" accessed November 17, 2023, https://www.gov.cn/zhengce/content/2015-05/08/content_9710.htm?trs=1.

9. General Office of the National Health Commission, "Letter From the General Office of the National Health and Wellness Commission Informing About the Assessment of County Hospitals' Medical Service Capacity in 2021–2022 (in Chinese) [EB/OL]" accessed November 17, 2023, http://www.nhc.gov.cn/yzygj/s3594q/202305/d87cb253740048ef98af1f37f67adba2.shtml.

10. General Office of the National Health and Family Planning Commission, Office of the State Administration of Traditional Chinese Medicine, "Circular on the Issuance of a Technical Program for Hierarchical Diagnosis and Treatment of Breast and Thyroid Cancer (in Chinese) [EB/OL]," published December 29, 2016, http://www.nhc.gov.cn/yzygj/s3594q/201702/0c46c23dc2694973bb5bea8060f1ccff.shtml.

11. Breast Committee of Chinese Research Hospital Association, Consensus Expert Group on Breast Cancer Prevention Among Chinese Women, "Expert Consensus on Women Breast Cancer Prevention in China (in Chinese)," *Journal of Chinese Research Hospitals* 9, no. 4 (2022): 5–13, https://doi.org/10.19450/j.cnki.jcrh.2022.04.003.

12. Medical Policy and Administration Agency, National Health Commission of the People's Republic of China, "Breast Cancer Treatment Guidelines (2022 Edition) (in Chinese)," *Chinese Journal of Oncology* 45, no. 10 (2023): 803–833, https://doi.org/10.3760/cma.j.cn112152-20230706-00281.

13. National Cancer Center, National Center for Oncology Quality Control, *Chinese Norms for Breast Cancer Screening and Early Diagnosis and Treatment (2019 Edition)* (People's Health Publishing House, 2020).

14. The Society of Breast Cancer China Anti-Cancer Association, "Guidelines for Breast Cancer Diagnosis and Treatment by China Anticancer Association (2021 Edition) (in Chinese)," *China Oncology* 31, no. 10 (2021): 954–1040, https://doi.org/10.19401/j.cnki.1007-3639.2021.10.013.

15. J. He, W. Q. Chen, N. Li, et al., "China Guideline for the Screening and Early Detection of Female Breast Cancer (2021, Beijing) (in Chinese)," *Chinese Journal of Oncology* 43, no. 4 (2021): 357–382, https://doi.org/10.3760/cma.j.cn112152-20210119-00061.

16. The Society of Breast Cancer China Anti-Cancer Association, "Screening and Early Diagnosis of Breast Cancer in China: A Practice Guideline (in Chinese)," *China Oncology* 32, no. 4 (2022): 363–372, https://doi.org/10.19401/j.cnki.1007-3639.2022.04.010.

17. Guidelines Working Committee of the Chinese Society of Clinical Oncology, *Chinese Society of Clinical Oncology (CSCO) Breast Cancer Guidelines 2023* (People's Health Publishing House, 2023).

18. B. H. Xu, S. S. Wang, Z. F. Jiang, et al., "Expert Consensus on Maintenance Therapy for Advanced Breast Cancer in China (in Chinese)," *National Medical Journal of China* 98, no. 2 (2018): 87–90, https://doi.org/10.3760/cma.j.issn.0376-2491.2018.02.003.

19. Breast Cancer Expert Committee of National Cancer Quality Control Center, Health Management Professional Committee of Beijing Breast Cancer Prevention and Control Society, "Comprehensive Management Guideline for Breast Cancer Follow-Up and Healthcare (2022 Edition) (in Chinese)," *Chinese Journal of Oncology* 44, no. 1 (2022): 1–28, https://doi.org/10.3760/cma.j.cn112152-20211029-00798.

20. Breast Cancer Expert Committee of National Cancer Quality Control Center, Cancer Drug Clinical Research Committee of China Anti-Cancer Association, "Consensus Recommendations for the Clinical Application of CDK4/6 Inhibitors in Patients With Hormone Receptor Positive, Human Epidermal Growth Factor Receptor 2 Negative Advanced Breast Cancer (in Chinese)," *Chinese Journal of Oncology* 43, no. 4 (2021): 405–413, https://doi.org/10.3760/cma.j.cn112152-20210113-00045.

21. The Society of Chemotherapy, Chinese Anti-Cancer Association; Committee of Neoplastic Supportive-Care (CONS), China Anti-Cancer Association, "A Consensus on the Clinical Diagnosis, Treatment, and Prevention of Cancer- and Chemotherapy-Related Anemia in China (2019 Edition) (in Chinese)," *Chinese Clinical Oncology* 46, no. 17 (2019): 869–875, https://doi.org/10.3969/j.issn.1000-8179.2019.17.919.

22. Society of Chemotherapy, China Anti-Cancer Association, Committee of Neoplastic Supportive-Care, China Anti-Cancer Association, "Consensus on the Clinical Diagnosis, Treatment and Prevention of Cancer Treatment-Induced Thrombocytopenia in China (2023 Edition) (in Chinese)," *National Medical Journal of China* 103, no. 33 (2023): 2579–2590, https://doi.org/10.3760/cma.j.cn112137-20230409-00575.

23. China Anti-Cancer Association Tumor Clinical Chemotherapy Professional Committee, China Anti-Cancer Association Tumor Support Therapy Professional Committee, "Consensus on Clinical Diagnosis, Treatment, and Prevention of Chemotherapy-Induced Neutropenia in China (2023 Edition) (in Chinese)," *Chinese Journal of Oncology* 45, no. 7 (2023): 575–583, https://doi.org/10.3760/cma.j.cn112152-20230224-00076.

24. Chinese Association of Anti-Cancer Society, Tumor Supportive Therapy Committee, "Chinese Expert Consensus on Prevention and Treatment of Nausea and Vomiting Associated With Tumor Drug Therapy (2022 Edition) (in Chinese)," *National Medical Journal of China* 102, no. 39 (2022): 3080–3094, https://doi.org/10.3760/cma.j.cn112137-20220810-01724.

25. General Office of the National Health and Family Planning Commission, "Circular of the General Office of the National Health and Family Planning Commission on the Issuance of Basic and Recommended Standards for the Medical Service Capacity of County Hospitals (in Chinese) [EB/OL]," published April 4, 2016, http://www.nhc.gov.cn/yzygj/s3594q/201605/b2b3a61a9382473f92ff949fcb817912.shtml.

26. National Health Commission, Chinese Medicine Council, State Administration of Traditional Chinese Medicine, "Notice of the Health Commission of the State Administration of Traditional Chinese Medicine on the Issuance of Internet Diagnosis and Treatment Management Measures (for Trial Implementation) and Three Other Documents (in Chinese) [EB/OL]," published July 17, 2018, https://www.gov.cn/gongbao/content/2019/content_5358684.htm.

27. E. E. Bright, L. B. Finkelstein, M. S. Nealis, et al., "A Systematic Review and Meta-Analysis of Interventions to Promote Adjuvant Endocrine Therapy Adherence Among Breast Cancer Survivors," *Journal of Clinical Oncology* 41, no. 28 (2023): 4548–4561, https://doi.org/10.1200/JCO.23.00697.

28. F. M. Eliassen, V. Blåfjelldal, T. Helland, et al., "Importance of Endocrine Treatment Adherence and Persistence in Breast Cancer Survivorship: A Systematic Review," *BMC Cancer* 23, no. 1 (2023): 625, https://doi.org/10.1186/s12885-023-11122-8.