Breast Cancer Recurrence – Clinician Perspective

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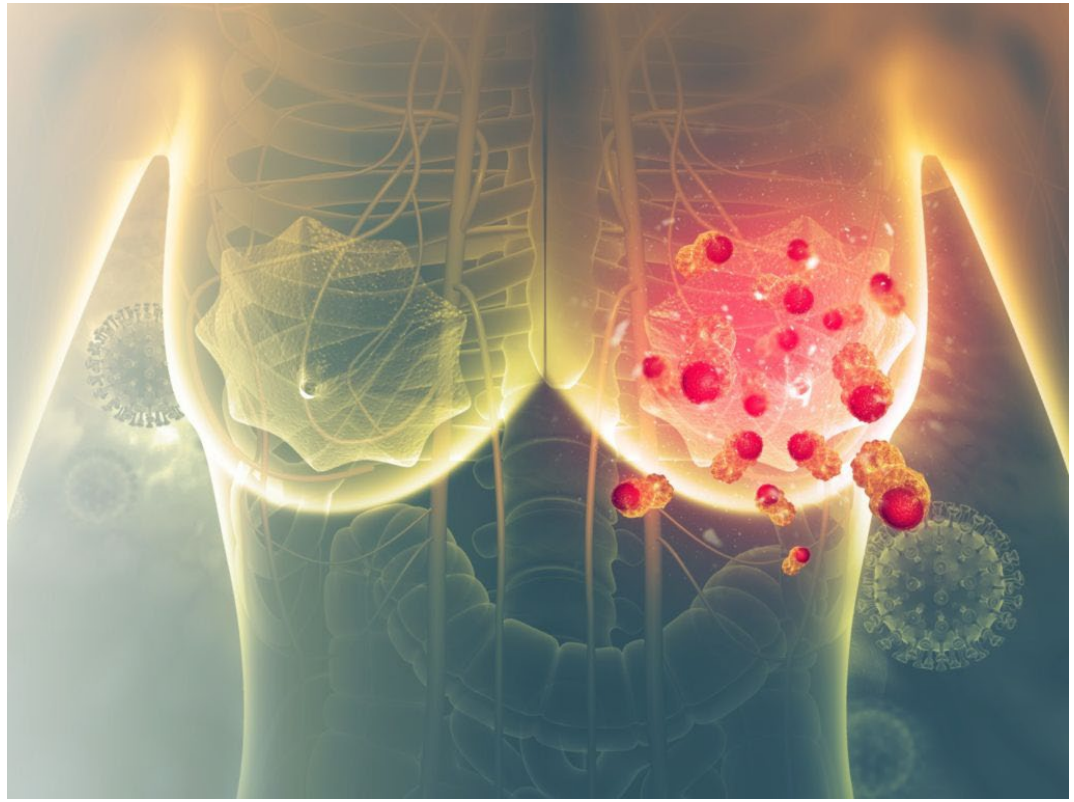
Objectives

- **Describe the clinical approaches used to diagnose breast cancer recurrence**, including the role of physical examination, imaging modalities (mammography, CT, MRI, PET), laboratory findings, and pathology in confirming recurrent disease.
- **Differentiate among local, regional, and distant breast cancer recurrence**, and distinguish recurrence from persistent or progressive disease using the concept of disease-free interval and clinical context.
- **Explain how patient risk factors and initial stage at diagnosis influence surveillance strategies and recurrence detection in clinical practice.**
- **Identify key medical record documentation and terminology used to support accurate abstraction of breast cancer recurrence**, including oncology progress notes, imaging and pathology reports, and treatment plans, while recognizing common documentation variations and pitfalls that impact registry coding accuracy.

Defining Recurrence

- NCI Dictionary
  - **Recurrent cancer:** “Cancer that has recurred (come back), usually after a period of time during which the cancer could not be detected. The cancer may come back to the same place as the original (primary) tumor or to another place in the body. Also called recurrence.”



Diagnosing Breast Cancer Recurrence

Objective: Describe the clinical approaches used to diagnose breast cancer recurrence, including the role of physical examination, imaging modalities (mammography, CT, MRI, PET), laboratory findings, and pathology in confirming recurrent disease.

NCCN Guidelines

National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2026
Invasive Breast Cancer

NCCN Guidelines Index
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Discussion

SURVEILLANCE/FOLLOW-UP

Exam:
- History and physical exam 1–4 times per year as clinically appropriate for 5 years, then annually

Genetic screening:
- Periodic screening for changes in family history and genetic testing indications and referral to genetic counseling as indicated, see NCCN Guidelines for Genetic/Familial High-Risk Assessment: Breast, Ovarian, Pancreatic, and Prostate

Postsurgical management:
- Educate, monitor, and refer for lymphedema management, see NCCN Guidelines for Survivorship: Lymphedema

Breast imaging:
- Mammography every 12 months, beginning 6 months or more after completion of breast-conservation therapy[ddd]
- Routine imaging of reconstructed breast is not indicated after mastectomy
- For patients with germline mutations or family history of breast cancer, please refer to NCCN Guidelines for Genetic/Familial High-Risk Assessment: Breast, Ovarian, Pancreatic, and Prostate

Fertility, birth control, and sexual health (see BINV-C)

Screening for metastases:
- In the absence of clinical signs and symptoms suggestive of recurrent disease, there is no indication for laboratory or imaging studies for metastases screening.

Post-treatment monitoring:
- Cardiotoxicity monitoring for patients who received left-sided RT, anthracyclines, or HER2-targeted therapy. For anthracycline-induced toxicity, see NCCN Guidelines for Survivorship
- Provide guidance on risk of comorbidities

Endocrine therapy:
- Assess and encourage adherence to adjuvant endocrine therapy
- Patients on tamoxifen:
  - Age-appropriate gynecologic screening
  - Routine annual pelvis ultrasound is not recommended
- Patients on an aromatase inhibitor or who experience ovarian failure secondary to treatment should have monitoring of bone health with a bone mineral density (BMD) determination at baseline and periodically thereafter[eee]

Lifestyle:
- Evidence suggests that active lifestyle, healthy diet, limited alcohol intake, and achieving and maintaining an ideal body weight (20–25 body mass index [BMI]) may lead to optimal breast cancer outcomes. See NCCN Guidelines for Breast Cancer Risk Reduction
- Menopausal hormone therapy is relatively contraindicated in survivors of hormonally mediated cancers; should be used with caution in those with increased genetic cancer risk. See NCCN Guidelines for Survivorship

Psychosocial support:
- Survivors are at elevated risk for fear of recurrence, distress, anxiety, and depression that may persist for many years after diagnosis. Periodic screening and referral to mental health professionals if needed are recommended. See NCCN Guidelines for Survivorship

Communication:
- Coordination of care between the primary care physician (PCP) and specialists is encouraged. Additionally, a personalized survivorship treatment plan including personalized treatment summary of possible long-term toxicity and clear follow-up recommendations is recommended. See NCCN Guidelines for Survivorship

Engagement:
- Patients frequently require follow-up encouragement in order to improve adherence to ongoing screening and medication adherence. See NCCN Guidelines for Patients

→ Recurrent Disease (BINV-18)

Diagnosing BC Recurrence: Physical Exam

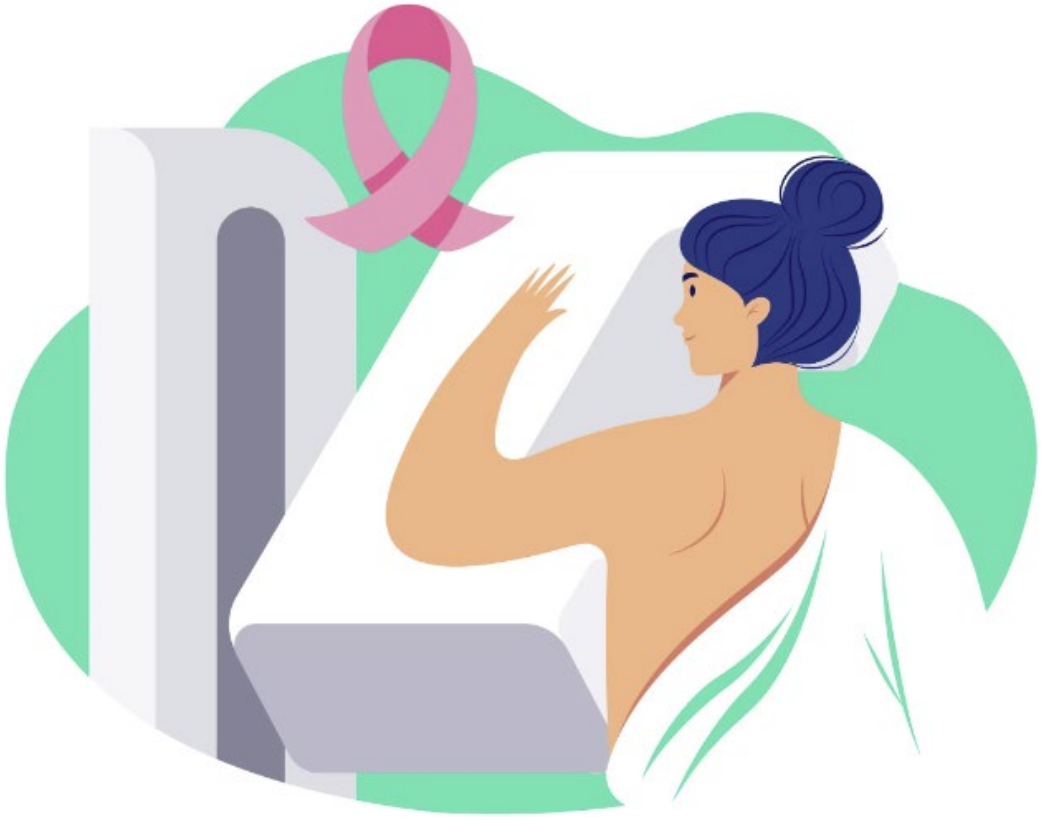
- NCCN: History and physical exam 1-4 times per year as clinically appropriate for 5 years, then annually

Diagnosing BC Recurrence: Imaging

- NCCN: Breast Imaging
  - Mammography every 12 months, beginning 6 months or more after completion of breast conservation therapy
  - Routine imaging of reconstructed breast is not indicated after mastectomy
  - For patients with germline mutations or family history of breast, refer to NCCN Guidelines for Genetic/Familial High-Risk
  - “The use of breast MRI in followup of patients with prior breast cancer is undefined. It may be considered as an option in patients with high lifetime risk (>20% based on models largely dependent on family history) of developing a second primary breast cancer. Rates of contralateral breast cancer after either breast-conserving therapy or mastectomy have been reported to be increased in patients with BRCA1/2 mutations when compared with patients with sporadic breast cancer.” ref 433-435

Diagnosing BC Recurrence: Imaging

- ASTRO Choosing Wisely
  - "…annual mammograms are the appropriate frequency for surveillance of breast cancer patients who have had BCS and RT with no clear advantage to shorter interval imaging. Patient should wait 6-12 months after completion of RT to begin their annual mammogram surveillance."



Diagnosing BC Recurrence: Imaging

- NCCN: Screening for Metastases
  - In the absence of clinical signs and symptoms suggestive of recurrence disease, there is no indication for laboratory or imaging studies for metastases screening

Diagnosing BC Recurrence: Imaging

- **Methods:** A literature search was conducted on the OvidSP platform in the MedLine database, using MeSH terms and subject headings related to breast cancer, brain metastases, and incidence. The search was conducted without language or publication restrictions, and included articles indexed from January 1, 2006 to June 10, 2018.
- **Results:** One hundred seventy studies were identified, with 33 included in the final analysis. Among nonmetastatic breast cancer patients, incidence of brain metastases as site of first recurrence per year of median follow-up ranged from 0.1% to 3.2%.
- **Conclusion:** In patients with nonmetastatic breast cancer, screening for asymptomatic brain metastases cannot currently be justified. However, due to the high incidence of brain metastases among patients with metastatic $HER2^+$ and triple-negative breast cancer, studies to determine the value of screening for brain metastases should be undertaken in these subgroups.

Diagnosing BC Recurrence: Imaging

- We retrospectively reviewed data of 398 patients who developed distant metastasis after their initial curative treatment between January 2000 and December 2015.
- Patients in the less-intensive surveillance group (LSG) had significantly longer relapse-free survival than did patients in the intensive surveillance group (ISG) (8.7 vs. 22.8 months; p = 0.002). While the ISG showed worse overall survival than the LSG did (50.2 vs. 59.9 months; p = 0.015), the difference was insignificant after adjusting for other prognostic factors. Among the 225 asymptomatic patients whose metastases were detected on imaging, the intensity of screening did not affect overall survival. A small subgroup of patients showed poor survival outcomes when they underwent intensive screening. Patients with HR-/HER2 + tumors and patients who developed lung metastasis in the LSG had better overall survival than those in the ISG did.
- Highly intensive screening for distant metastasis in disease-free patients with breast cancer was not associated with significant survival benefits, despite the recent improvements in therapeutic options and diagnostic techniques.

Diagnosing BC Recurrence: Lab Findings

- NCCN: Screening for Metastases
  - In the absence of clinical signs and symptoms suggestive of recurrence disease, there is no indication for laboratory or imaging studies for metastases screening
- NCCN: “The routine performance of alkaline phosphatase tests and LFTs are not included in the guidelines” ref 429-431
- “The panel notes no evidence to support the use of ‘tumor markers’ for breast cancer, and routine bone scans, CT scans, MRI scans, PET scans, or ultrasound examinations in the asymptomatic patient provide no advantage in survival or ability to palliate recurrent disease and are, therefore, not recommended.” ref 110, 432

Diagnosing BC Recurrence: Lab Findings

- **American Cancer Society/American Society of Clinical Oncology Breast Cancer Survivorship Care Guideline**
- A systematic review of the literature was conducted using PubMed through April 2015. A multidisciplinary expert workgroup with expertise in primary care, gynecology, surgical oncology, medical oncology, radiation oncology, and nursing was formed and tasked with drafting the Breast Cancer Survivorship Care Guideline. A total of 1,073 articles met inclusion criteria; and, after full text review, 237 were included as the evidence base. Patients should undergo regular surveillance for breast cancer recurrence, including evaluation with a cancer-related history and physical examination, and should be screened for new primary breast cancer. Data do not support performing routine laboratory tests or imaging tests in asymptomatic patients to evaluate for breast cancer recurrence.

Diagnosing BC Recurrence: Lab Findings

- Minimal Residual Disease
- ctDNA can:
  - Detect minimal residual disease
  - Predict relapse months-years before imaging
  - Highly prognostic
- ctDNA lacks clinical utility >> No prospective trials demonstrate that acting on ctDNA improves outcomes

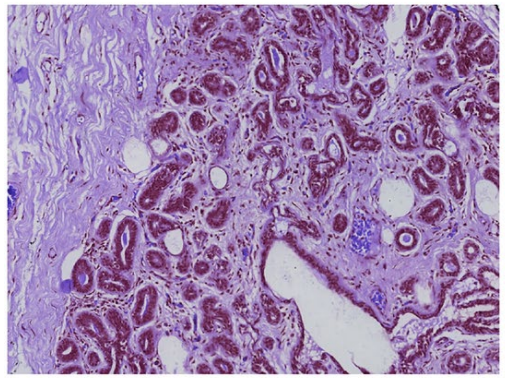
Defining Recurrence

- NCI Dictionary
  - **Recurrent cancer:** “Cancer that has recurred (come back), usually after a period of time during which the cancer could not be detected. The cancer may come back to the same place as the original (primary) tumor or to another place in the body. Also called recurrence.”

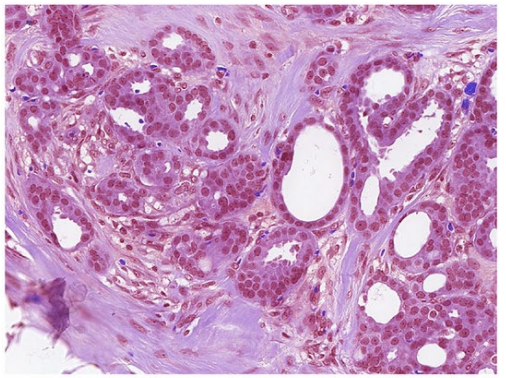
Diagnosing BC Recurrence: Pathology

- Diagnosis typically requires tissue confirmation
  - Same histology (ductal, lobular, etc)
  - Same biomarkers (ER, PR, HER2)
  - Local, regional, or distant
  - Genomic assays may also be helpful

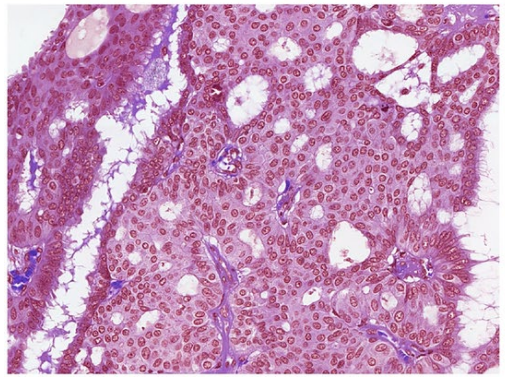
Normal



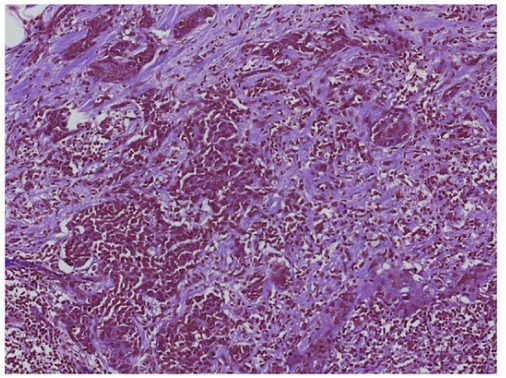
Benign



In situ carcinoma



Invasive carcinoma

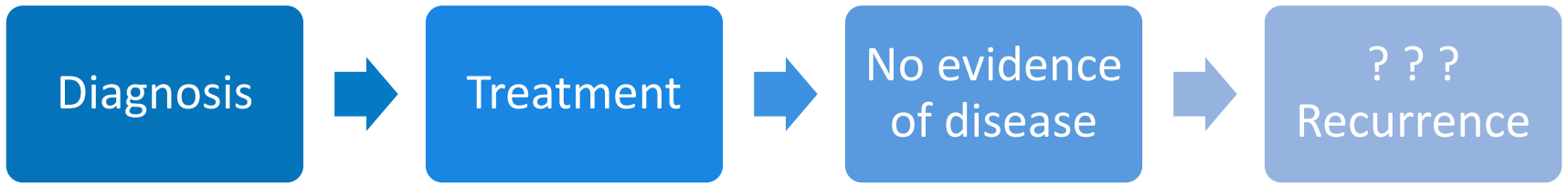


Differentiating recurrence from persistent/progressive disease

Objective: Differentiate among local, regional, and distant breast cancer recurrence, and distinguish recurrence from persistent or progressive disease using the concept of disease-free interval and clinical context.

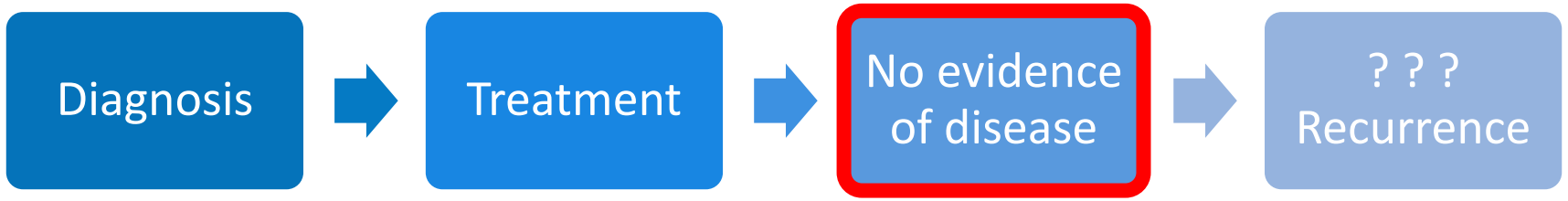
Defining Recurrence

- NCI Dictionary
  - **Recurrent cancer:** “Cancer that has recurred (come back), usually after a period of time during which the cancer could not be detected. The cancer may come back to the same place as the original (primary) tumor or to another place in the body. Also called recurrence.”



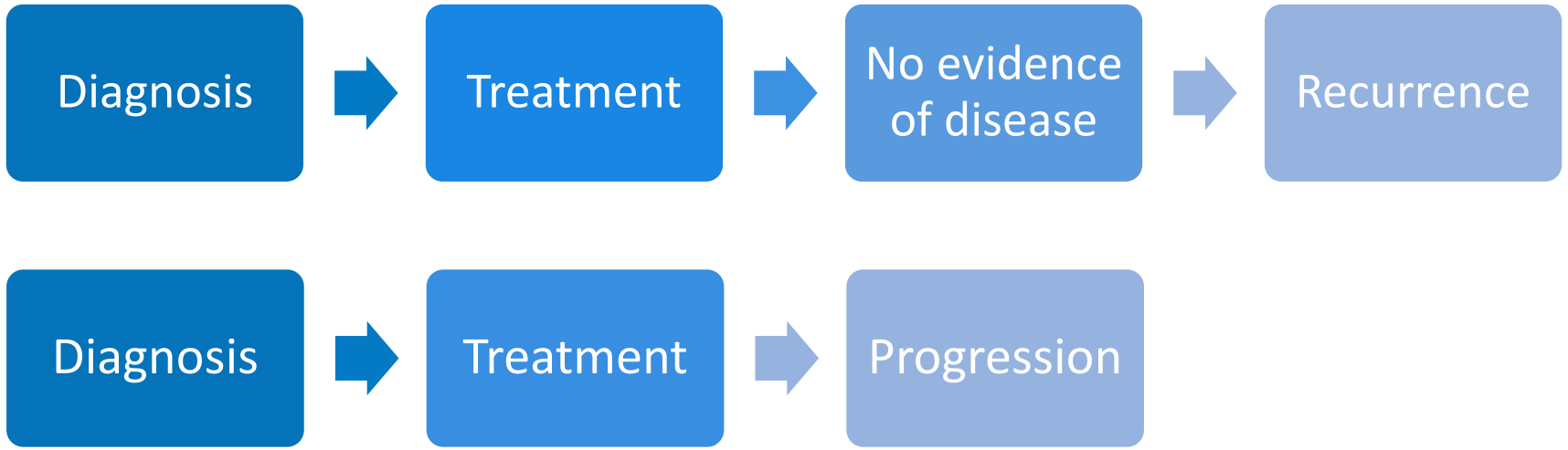
Recurrence vs Progression

- NCI Dictionary of Cancer Terms
  - **Disease-free Interval:** “In cancer, the length of time after primary treatment for a cancer ends that the patient survives without any signs or symptoms of that cancer. In a clinical trial, measuring the disease-free survival is one way to see how well a new treatment works. Also called DFS, relapse-free survival, and RFS.”



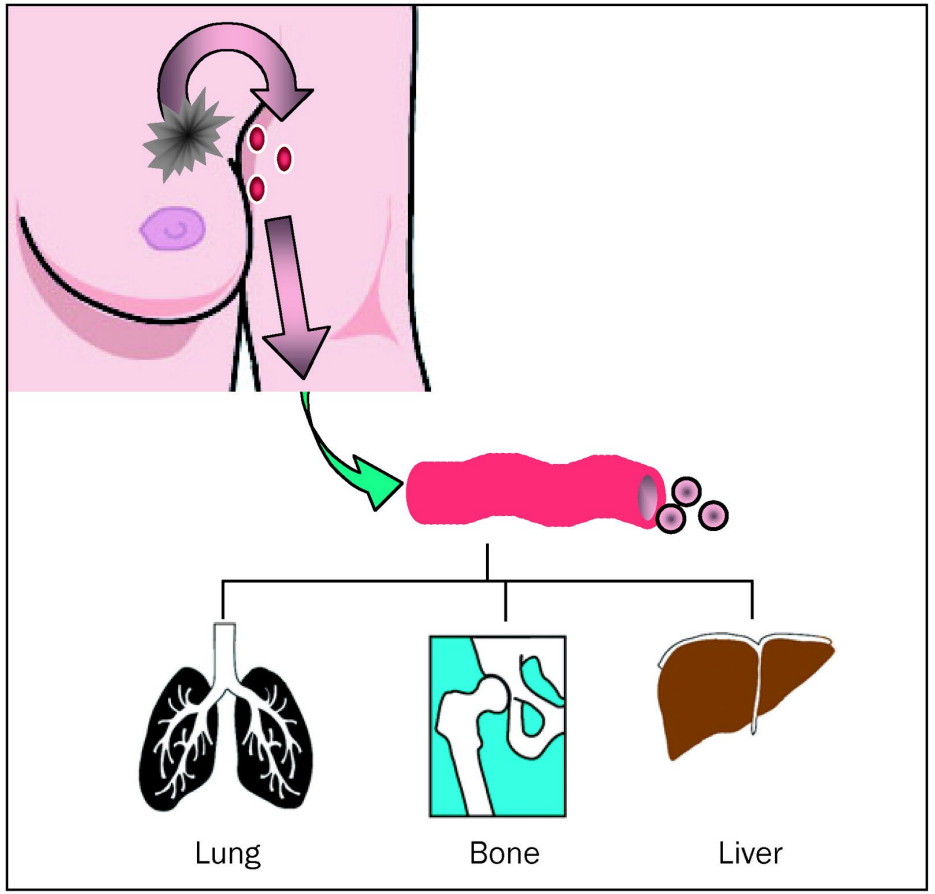
Recurrence vs Progression

- **Recurrence** means the cancer has come back.
- **Progression** means the cancer is growing or spreading without ever having gone away completely.



Recurrence vs Progression

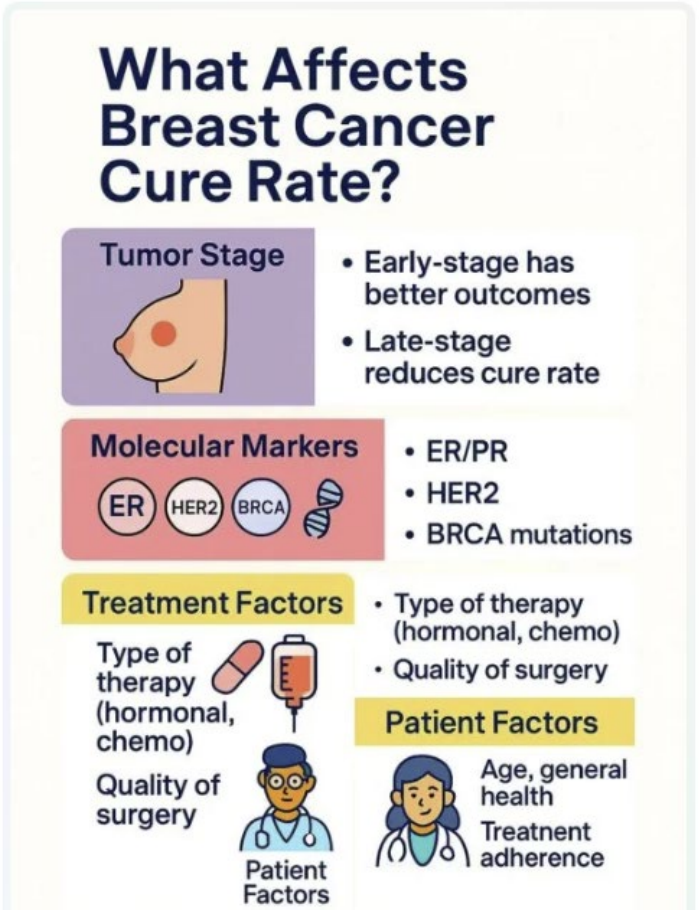
- **NCI: Recurrent Cancer: When Cancer Comes Back**
- **Types of Recurrent Cancer**
  - Local recurrence means that the cancer is in the same place as the original cancer or very close to it.
  - Regional **recurrence** means that the tumor has grown into lymph nodes or tissues near the original cancer.
  - **Distant recurrence** means the cancer has spread to organs or tissues far from the original cancer. When cancer spreads to a distant place in the body, it is called metastasis or metastatic cancer. When cancer spreads, it is still the same type of cancer. For example, if you had colon cancer, it may come back in your liver. But, the cancer is still called colon cancer.

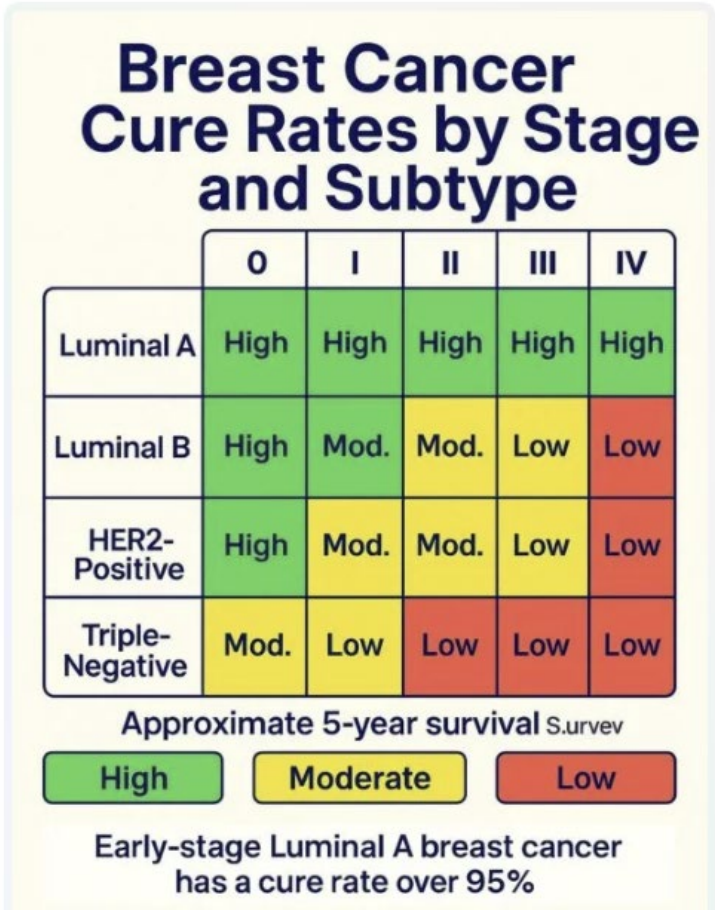


Considers for surveillance strategies and recurrence detection

Objective: Explain how patient risk factors and initial stage at diagnosis influence surveillance strategies and recurrence detection in clinical practice.

Predicting BC Recurrence





	0	I	II	III	IV
Luminal A	High	High	High	High	High
Luminal B	High	Mod.	Mod.	Low	Low
HER2-Positive	High	Mod.	Mod.	Low	Low
Triple-Negative	Mod.	Low	Low	Low	Low

Predicting BC Recurrence: HR+ Disease

- **Methods:** In this meta-analysis of the results of 88 trials involving 62,923 women with ER-positive breast cancer who were disease-free after 5 years of scheduled endocrine therapy, we used Kaplan-Meier and Cox regression analyses, stratified according to trial and treatment, to assess the associations of tumor diameter and nodal status (TN), tumor grade, and other factors with patients' outcomes during the period from 5 to 20 years.
- **Results:** Breast-cancer recurrences occurred at a steady rate throughout the study period from 5 to 20 years.
- The risk of distant recurrence was strongly correlated with the original TN status. Among the patients with stage T1 disease, the risk of distant recurrence was 13% with no nodal involvement (T1N0), 20% with one to three nodes involved (T1N1-3), and 34% with four to nine nodes involved (T1N4-9); among those with stage T2 disease, the risks were 19% with T2N0, 26% with T2N1-3, and 41% with T2N4-9.
- The risk of death from breast cancer was similarly dependent on TN status.
- Given the TN status, the factors of tumor grade (available in 43,590 patients) and Ki-67 status (available in 7692 patients), which are strongly correlated with each other, were of only moderate independent predictive value for distant recurrence, but the status regarding the progesterone receptor (in 54,115 patients) and human epidermal growth factor receptor type 2 (HER2) (in 15,418 patients in trials with no use of trastuzumab) was not predictive.
- During the study period from 5 to 20 years, the absolute risk of distant recurrence among patients with T1N0 breast cancer was 10% for low-grade disease, 13% for moderate-grade disease, and 17% for high-grade disease; the corresponding risks of any recurrence or a contralateral breast cancer were 17%, 22%, and 26%, respectively.
- **Conclusions:** After 5 years of adjuvant endocrine therapy, breast-cancer recurrences continued to occur steadily throughout the study period from 5 to 20 years. The risk of distant recurrence was strongly correlated with the original TN status, with risks ranging from 10 to 41%, depending on TN status and tumor grade.

Table 1: Risk of Distant Recurrence 10 to 20 Years After Diagnosis and Discontinuation of Endocrine Therapy at 5 Years

Tumor Subgroup	10 Years	15 Years	20 Years
T1N0	4%	9%	14%
T1N1 (1–3 nodes)	8%	15%	23%
T1N2 (4–9 nodes)	16%	30%	41%
T2N0	8%	14%	21%
T2N1 (1–3 nodes)	12%	20%	29%
T2N2 (4–9 nodes)	20%	35%	47%

BC Surveillance (Recurrence Screening)

- NCCN: Screening for Metastases
  - In the absence of clinical signs and symptoms suggestive of recurrence disease, there is no indication for laboratory or imaging studies for metastases screening
- NCCN: “The routine performance of alkaline phosphatase tests and LFTs are not included in the guidelines” ref 429-431
- “The panel notes no evidence to support the use of ‘tumor markers’ for breast cancer, and routine bone scans, CT scans, MRI scans, PET scans, or ultrasound examinations in the asymptomatic patient provide no advantage in survival or ability to palliate recurrent disease and are, therefore, not recommended.” ref 110, 432

Medical Record Documentation related to Breast Cancer Recurrence

Objective: Identify key medical record documentation and terminology used to support accurate abstraction of breast cancer recurrence, including oncology progress notes, imaging and pathology reports, and treatment plans, while recognizing common documentation variations and pitfalls that impact registry coding accuracy.

Key Documentation and Terminology

- key medical record documentation and terminology used to support accurate abstraction of breast cancer recurrence,
- No evidence of disease/malignancy (oncology progress notes)
- Normal/negative imaging
- Normal bloodwork

- including oncology progress notes, imaging and pathology reports, and treatment plans, while recognizing common documentation variations and pitfalls that impact registry coding accuracy.

Documentation Pitfalls

- Differentiating recurrence vs progression
  - Requires a disease-free interval
- Differentiating recurrence vs new primary
  - Differences in histology, biomarkers
  - Disease isolated to breast and/or lymph nodes

Questions?

Thank you!

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