



National
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NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

Breast Cancer Screening and Diagnosis

Version 1.2015

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NCCN Guidelines Version 1.2015 Panel Members

Breast Cancer Screening and Diagnosis

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[Discussion](#)

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† Medical oncology
‡ Hematology/Hematology oncology
‡ Internist/Internal medicine, including family
practice, preventive management
Ω Gynecologic oncology/Gynecology
#Pathology
¥ Patient advocacy
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Clinical Trials: NCCN believes that the best management for any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

To find clinical trials online at NCCN Member Institutions, [click here: nccn.org/clinical_trials/physician.html](#).

NCCN Categories of Evidence and Consensus: All recommendations are category 2A unless otherwise specified.

See [NCCN Categories of Evidence and Consensus](#).

The NCCN Guidelines® are a statement of evidence and consensus of the authors regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult the NCCN Guidelines is expected to use independent medical judgment in the context of individual clinical circumstances to determine any patient's care or treatment. The National Comprehensive Cancer Network® (NCCN®) makes no representations or warranties of any kind regarding their content, use or application and disclaims any responsibility for their application or use in any way. The NCCN Guidelines are copyrighted by National Comprehensive Cancer Network®. All rights reserved. The NCCN Guidelines and the illustrations herein may not be reproduced in any form without the express written permission of NCCN. ©2015.

NCCN Guidelines Version 1.2015 Updates

Breast Cancer Screening and Diagnosis

Updates in Version 1.2015 of the NCCN Guidelines for Breast Cancer Screening from Version 1.2014 include:

BSCR-1

- ~~"Lobular carcinoma in situ (LCIS) or ADH/ALH"~~ has been deleted.
- Modified 5th bullet to read: Women who have a lifetime risk >20% based on history of LCIS or ADH/ALH (Also for BSCR-2).
- 5th bullet has been modified to include (eg, mantle irradiation).
- Footnote "a" See Breast Screening Considerations (BSCR-A), corresponds to "Clinical breast exam."
- Age ≥35 Years was added to footnote "d" (Also for BSCR-2)
- "Periodic, consistent breast self exam (BSE) may facilitate breast self awareness. Premenopausal women may find BSE most informative when performed at the end of menses" has been deleted from footnote "g" (Also for BSCR-2).
- The original footnote "g" has been modified and has been moved to be the second bullet on BSCR-A: "Adequate clinical breast exams include the following: upright and supine position during inspection exam, ~~appearance of breast, and~~ palpation of all components of the breast, axilla, and clavicular lymph node basins. Time spent on the palpable portion of the exam is associated with increased detection of palpable abnormalities. O'clock location and distance from nipple facilitate geographic correlation with imaging findings."

BSCR-2

- "to begin at diagnosis but not less than age 30 y" was added as a sub-bullet to "annual screening mammogram"
- "Consider annual MRI to begin at diagnosis but not less than age 30 y (based on emerging evidence)" is new and corresponds to "Women who have a lifetime risk >20% based on history of LCIS or ADH/ALH."
- For annual screening mammogram and annual breast MRI the following has been added, "begin 10 years prior to youngest family member but not less than age 30 y"
- "Current age" has been added to "<25 y" and "≥25 y" pathway.

BSCR-2

- Footnote "i" has been modified: "Randomized trials comparing clinical breast exam versus no screening have not been performed. Rationale for recommending clinical breast exam every 6–12 mo is the concern for early detection of interval breast cancers."

BSCR-3

5th column changed "Initial Evaluation" to "Diagnostic Evaluation" for all pathways.

BSCR-4

- Changed page title to, "Diagnostic Evaluation" from "Initial Evaluation."
- Deleted "± ultrasound as needed" from Diagnostic Mammogram.
- 3rd column: added "Mammogram" to BI-RADS categories upper pathway off mammogram, "Ultrasound" was added for clarity, lower pathway off mammogram, "Consider ultrasound for biopsy for guidance and lesion size"

BSCR-5

- "Tissue sampling may be appropriate if clinically suspicious, aids in management, or is strongly desired by patient" is a new footnote that corresponds to BI-RADS category 3. (Also for BSCR 11 and 13)
- 3rd column top pathway, "Observation (with for low clinical suspicion)."
 - Upper pathway, off "Solid/Probably benign finding": Tissue biopsy has been modified to include, "for intermediate or high level of clinical suspicion." (Also for BSCR 6 and 11)
- "Physical exam ± ultrasound/diagnostic mammogram every 6-12 mo, for 1-2 -"3" y to assess stability."
- 5th column top pathway modified: "Significant increase in size or suspicion" this change has been made throughout the guidelines.
- 6th column top pathway modified: "Tissue biopsy" has a corresponding footnote, "FNA and core (needle or vacuum-assisted) biopsy are both valuable. FNA requires cytologic expertise. Surgical excision is appropriate if unable to perform core needle biopsy or if strongly desired by patient."
- Bottom pathway, deleted "~~Image-guided biopsy~~" and its corresponding footnote.

NCCN Guidelines Version 1.2015 Updates

Breast Cancer Screening and Diagnosis

Updates in Version 1.2015 of the NCCN Guidelines for Breast Cancer Screening from Version 1.2014 include:

BSCR-6

- 2nd column, top pathway has been modified: "Observe (for low clinical suspicion) ~~every 3–6 mo ± imaging for 1–2 y to assess stability for mammographic findings as needed.~~"

BSCR-7

- 3rd column, top pathway "diagnostic" has been deleted. Pathway now reads, "Physical exam ± ultrasound/~~diagnostic~~ mammogram every 6–12 mo for 1–2 y^V to assess stability for imaging findings as needed."

BSCR-8

"*Pleomorphic LCIS should be managed according to the NCCN Guidelines for Breast Cancer*" is a new footnote corresponding to LCIS

BSCR-9

- After aspiration, 2nd column, middle pathway, "and nonbloody fluid" has been deleted to now read, "*Mass resolves/Screening/Mass recurs/US or Surgical excision.*"
- 2nd column bottom pathway beginning with "Mass resolves and bloody fluid" has been deleted as well as the entire branch.

BSCR-10

- Title of the page, "Initial Evaluation" has been changed to "*Diagnostic Evaluation.*"
- 2nd column, bottom pathway has been modified: "*Observe for low clinical suspicion for 1-2 menstrual cycles*"

BSCR-11

- 2nd column, upper pathway "*diagnostic*" was added before imaging and footnote "u" was added to 1–2 years.
- Pathway off BI-RADS category 3 has been modified: "Physical exam every 3–6 mo and diagnostic *imaging* every 6–12 mo for 1–2 "3"y to assess stability for low clinical suspicion"
- "*Imaging*" replaces "~~mammogram~~" throughout the page

BSCR-12

- 2nd column, bottom pathway modified: "Persistent and reproducible on exam, spontaneous, unilateral, single duct, ~~and clear and colorless~~, serous, sanguineous, or serosanguineous."
- 4th column, pathway off Age ≥40 y, 1st bullet modified: "Diagnostic mammogram + *ultrasound*, if not done recently."
 - ▶ BI-RADS category 1-3 has new corresponding footnote, "*If BI-RADS Category 3 finding is unrelated to nipple discharge, manage mammographic finding by BSCR-15.*"
- 6th column:
 - ▶ the 3 BI-RADS nodes off MRI (optional) are new to the page.
 - ▶ bottom pathway, "*Tissue biopsy*" is new to the page.
 - ▶ bottom pathway off Benign, "*Clinical correlation to determine need for duct excision*" is new to the page
 - ▶ 7th column, lower pathway: "*Duct excision*" or "*6-mo follow-up physical exam and imaging for 1–2 y*" are two new pathways off Ductogram or MRI.

BSCR-14

- Footnote "cc" has been modified: "If clinically of low suspicion for breast cancer or high suspicion for infection, a short trial (7–10 days) of antibiotics for mastitis may be indicated."

BSCR-15

- 3rd column under "Diagnostic Follow-up," has been modified: "Diagnostic workup including comparison to prior films and/or diagnostic mammogram ± *and/or* ultrasound as indicated"
 - ▶ Pathway off BI-RADS category 3 probably benign finding has been modified: "Diagnostic mammogram at 6 mo, then every 6–12 mo for 1–2 "3" y."

BSCR-16

- The title of the page has been modified: "Follow-up after diagnostic *imaging*"
- The pathway off "Pathology/image discordant" has been deleted. It now reads, "Pathology/image discordant/Surgical excision/Follow-up"



NCCN Guidelines Version 1.2015 Updates

Breast Cancer Screening and Diagnosis

Updates in Version 1.2015 of the NCCN Guidelines for Breast Cancer Screening from Version 1.2014 include:

[BSCR-A 1 of 2](#)

- 6th bullet has been modified: "There are several studies supporting the use of ~~ultrasound~~ supplemental screening for breast cancer screening as an adjunct to screening mammography for ~~high-risk women~~ with dense breast tissue. *Different modalities may be considered based on risk.*"
- 8th bullet has been modified: "Early studies show promise for tomosynthesis mammography. ~~Several studies~~ ~~Two large trials~~ show a combined use of digital mammography and tomosynthesis resulted in improved cancer detection and decreased call back rates. Of note, ~~this is~~ ~~most studies used~~ double the dose of radiation. ~~and is a factor in recommending this modality.~~ *The radiation dose can be minimized by synthetic 2-D reconstruction.* Definitive studies are still pending."

[BSCR-A 2 of 2](#)

- Under "Recommend Annual MRI Screening (Based on Evidence)":
 - ▶ to the 1st and 2nd bullets, "*commence at age 25 y*" is new to the page.
- "*Consider MRI screening for LCIS and ALH/ADH based on emerging evidence*" is new to the page.
 - ▶ The 2nd and 3rd bullets under "Insufficient Evidence to Recommend for or Against MRI Screening have been deleted and included in the new bullet above."

[BSCR-B](#)

- The title of the page has been modified to include, "Age ≥ 35 Years"

[BSCR-C 4 of 9 and 8 of 9](#)

- *The new BI-RADS® cut points defined for the risk of malignancy are as follows: 4A (>2% - $\leq 10\%$), 4B (>10% - $\leq 50\%$), 4C (>50% - <95%).*

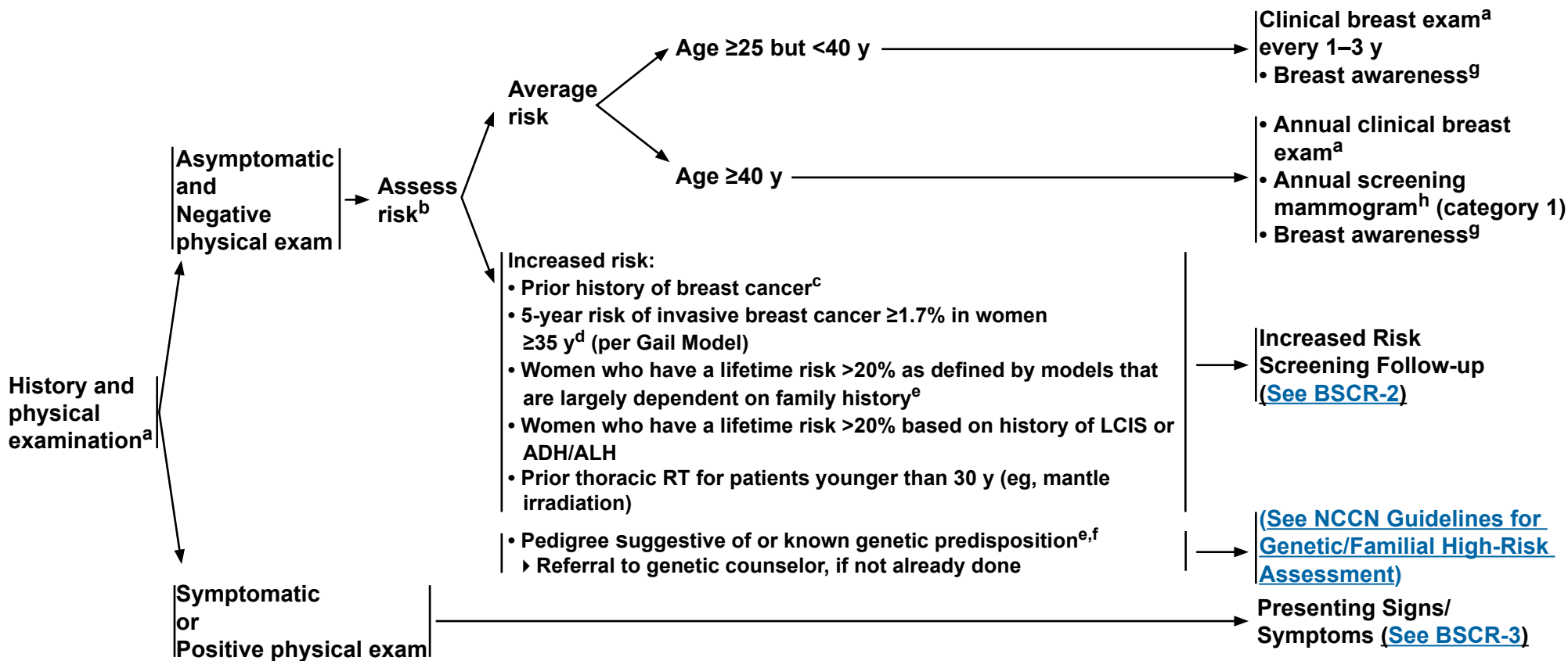


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Breast Cancer Screening and Diagnosis

SCREENING OR SYMPTOM CATEGORY

SCREENING/FOLLOW-UP^a



^aSee [Breast Screening Considerations \(BSCR-A\)](#).

^bRefer to the [NCCN Guidelines for Breast Cancer Risk Reduction](#) for a detailed qualitative and quantitative assessment.

^cSee [NCCN Guidelines for Breast Cancer - Surveillance Section](#).

^dSee [Risk Factors Used in the Modified Gail Model, Age ≥35 Years \(BSCR-B\)](#).

^eRisk models that are largely dependent on family history (eg, Claus, BRCA1/2, BOADICEA, Tyrer-Cuzick). See [NCCN Guidelines for Breast Cancer Risk Reduction](#).

^fThere is variation in recommendations for initiation of screening for different genetic syndromes. See [NCCN Guidelines for Genetic/Familial High-Risk Assessment: Breast and Ovarian](#).

^gWomen should be familiar with their breasts and promptly report changes to their health care provider.

^hSee [Mammographic Evaluation \(BSCR-15\)](#).

Note: All recommendations are category 2A unless otherwise indicated.

Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.



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Breast Cancer Screening and Diagnosis

SCREENING OR SYMPTOM CATEGORY

SCREENING/FOLLOW-UP

Increased Risk:

Prior history of breast cancer

→ [See NCCN Guidelines for Breast Cancer - Surveillance Section](#)

Women ≥35 y with 5-year risk of
invasive breast cancer ≥1.7%^d

- Annual screening mammogram^h + clinical breast exam^a every 6–12 moⁱ
 - ▶ to begin at diagnosis but not less than age 30 y
- Breast awareness^g
- Consider risk reduction strategies ([See NCCN Guidelines for Breast Cancer Risk Reduction](#))

OR

Women who have a lifetime risk
>20% based on history of LCIS or
ADH/ALH

- Annual screening mammogram^h + clinical breast exam^a every 6–12 moⁱ
 - ▶ to begin at diagnosis but not less than age 30 y
- Breast awareness^g
- Consider risk reduction strategies ([See NCCN Guidelines for Breast Cancer Risk Reduction](#))
- Consider annual MRI
 - ▶ to begin at diagnosis but not less than age 30 y (based on emerging evidence)

OR

Women who have a lifetime risk
>20% as defined by models that are
largely dependent on family history^e

- Annual screening mammogram^h + clinical breast exam^a every 6–12 moⁱ
 - ▶ to begin 10 years prior to youngest family member but not less than age 30 y
- Breast awareness^g
- Consider risk reduction strategies ([See NCCN Guidelines for Breast Cancer Risk Reduction](#))
- Recommend annual breast MRI^j
 - ▶ to begin 10 years prior to youngest family member but not less than age 30 y
- Referral to genetic counseling if not already done

Prior thoracic RT
between the ages of
10 and 30 y

Current age <25 y →

- Annual clinical breast exam^a
 - ▶ beginning 8–10 y after RT
- Breast awareness^g

Current age ≥25 y →

- Annual screening mammogram^h + clinical breast exam^a every 6–12 moⁱ
 - ▶ Begin 8–10 y after RT
- Recommend annual breast MRI^j
- Breast awareness^g

^a[See Breast Screening Considerations \(BSCR-A\)](#)

^d[See Risk Factors Used in the Modified Gail Model, Age ≥35 Years \(BSCR-B\)](#)

^eRisk models that are largely dependent on family history (eg, Claus, BRCAPRO, BOADICEA, Tyrer-Cuzick). [See NCCN Guidelines for Breast Cancer Risk Reduction](#).

^gWomen should be familiar with their breasts and promptly report changes to their health care provider.

^hSee Mammographic Evaluation ([BSCR-15](#)).

ⁱRandomized trials comparing clinical breast exam versus no screening have not been performed. Rationale for recommending clinical breast exam every 6–12 mo is the concern for early detection of interval breast cancers.

^jHigh-quality breast MRI limitations include having: a need for a dedicated breast coil, the ability to perform biopsy under MRI guidance, experienced radiologists in breast MRI, and regional availability. Breast MRI is performed preferably days 7–15 of menstrual cycle for premenopausal women. MRI should be integrated with other breast imaging modalities.

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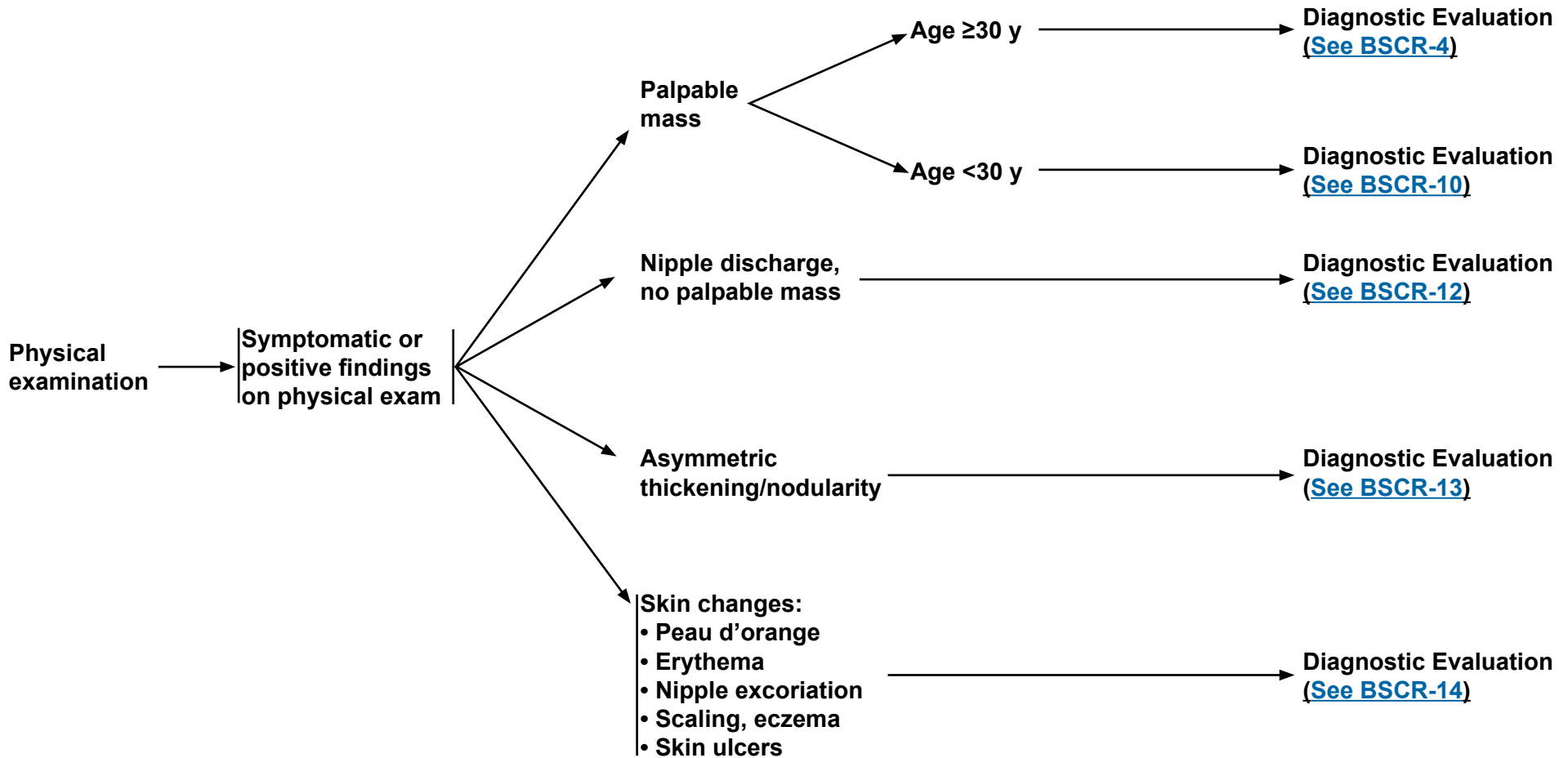
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Breast Cancer Screening and Diagnosis

PRESENTING SIGNS/SYMPTOMS



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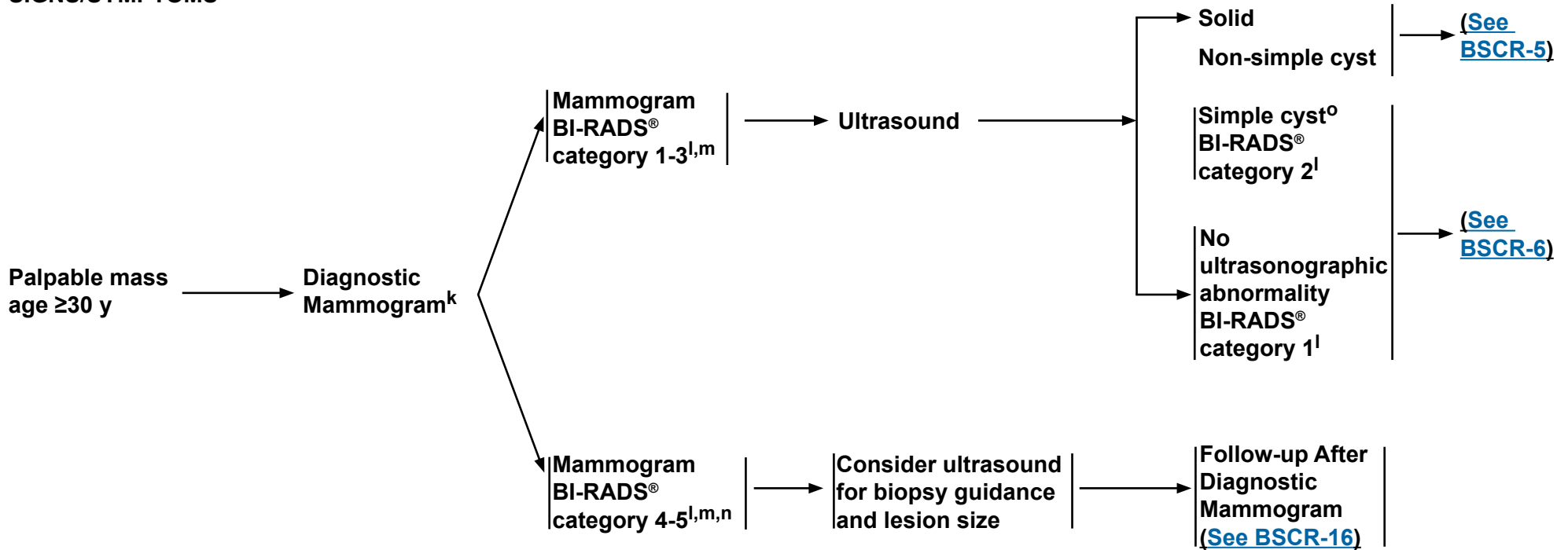
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Breast Cancer Screening and Diagnosis

PRESENTING SIGNS/SYMPTOMS

DIAGNOSTIC EVALUATION

ULTRASOUND FINDINGS



^kThere are some clinical circumstances such as mass with low clinical suspicion or suspected simple cyst in which ultrasound would be preferred and may suffice for women 30–39 years of age. [See Discussion section.](#)

^l[See Assessment Category Definitions \(BSCR-C\).](#)

^mMammography results are mandated to be reported using Final Assessment categories (Quality Mammography Standards: Final Rule. Federal Register. 1997;62:55988).

ⁿAssess geographic correlation between clinical and imaging findings. If there is a lack of correlation, return to Category 1-3 for further workup of palpable lesion. If imaging findings correlate with the palpable finding, workup of the imaging problem will answer the palpable problem.

^oConcordance is needed between clinical exam and ultrasound results. Consider therapeutic aspiration for persistent clinical symptoms.

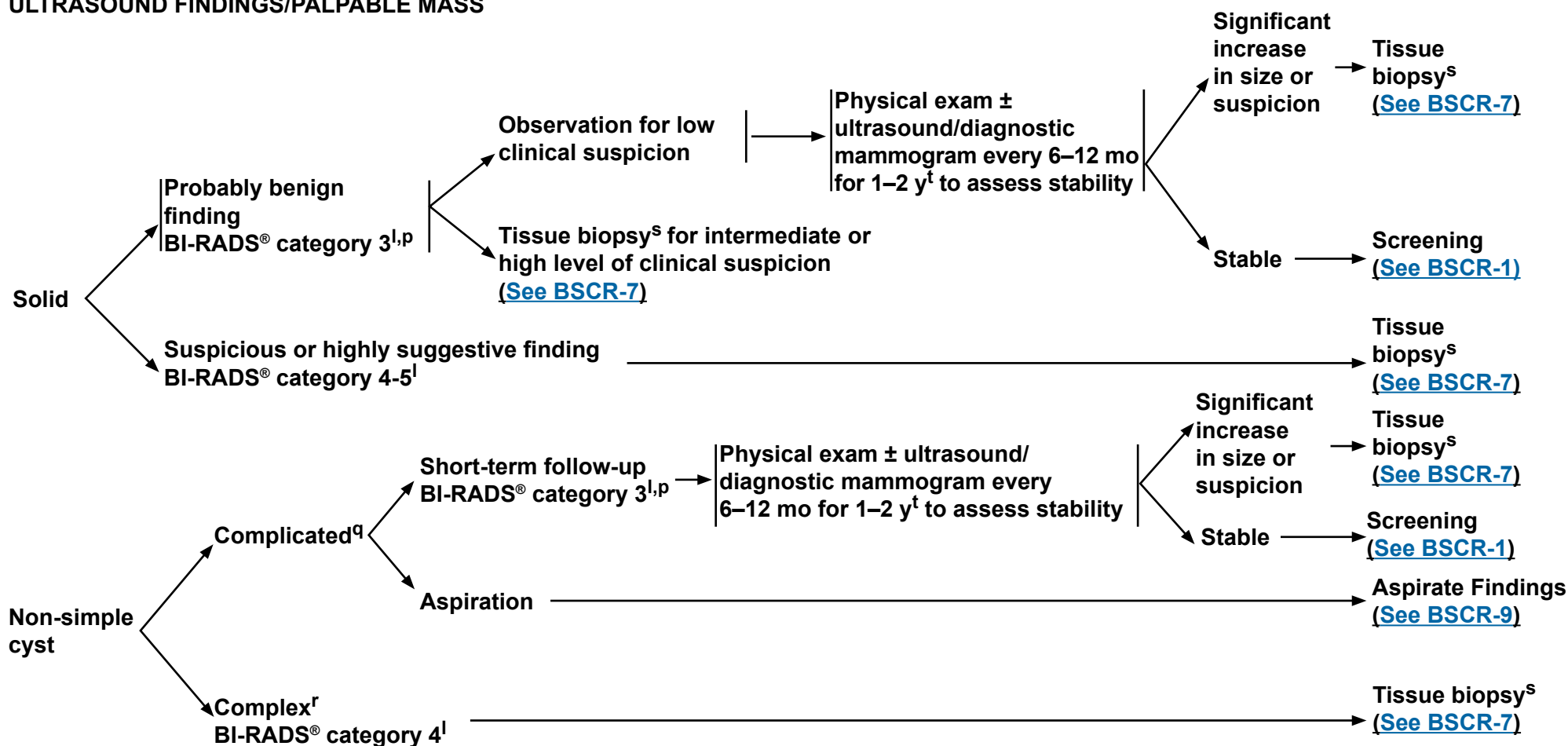
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Breast Cancer Screening and Diagnosis

ULTRASOUND FINDINGS/PALPABLE MASS



^lSee Assessment Category Definitions (BSCR-C).

^pTissue sampling may be appropriate if clinically suspicious, aids in management, or is strongly desired by patient.

^qRound, circumscribed mass containing low-level echoes without vascular flow, fulfilling most but not all criteria for simple cyst.

^rA complex cyst has both cystic and solid components.

^sFNA and core (needle or vacuum-assisted) biopsy are both valuable. FNA requires cytologic expertise. Surgical excision is appropriate if unable to perform core needle biopsy or if strongly desired by patient.

^tThere may be variability on the follow-up interval based on the level of suspicion.

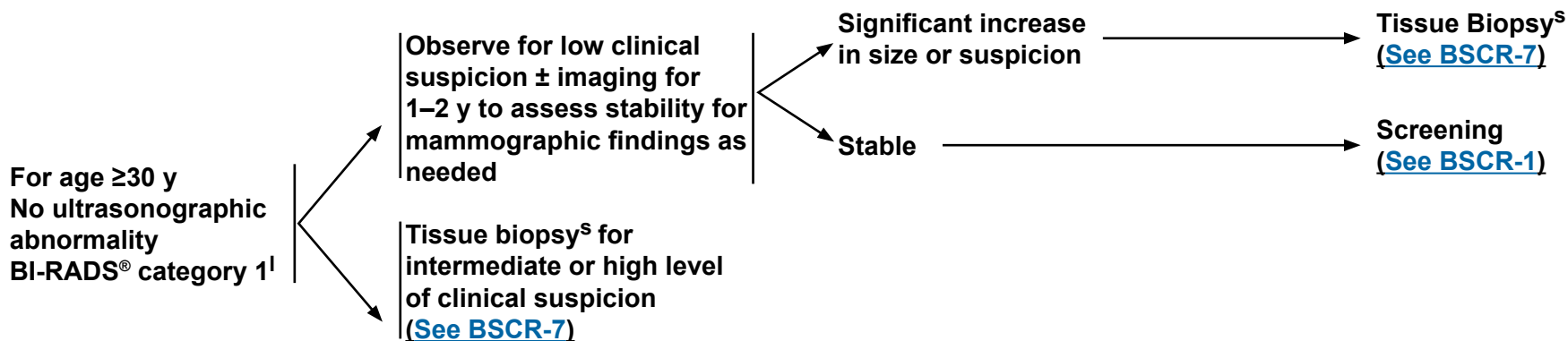
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ULTRASOUND FINDINGS/PALPABLE MASS

Simple cyst^o
BI-RADS® category 2^l → Screening ([See BSCR-1](#))



^lSee Assessment Category Definitions (BSCR-C).

^oConcordance is needed between clinical exam and ultrasound results. Consider therapeutic aspiration for persistent clinical symptoms.

^sFNA and core (needle or vacuum-assisted) biopsy are both valuable. FNA requires cytologic expertise. Surgical excision is appropriate if unable to perform core needle biopsy or if strongly desired by patient.

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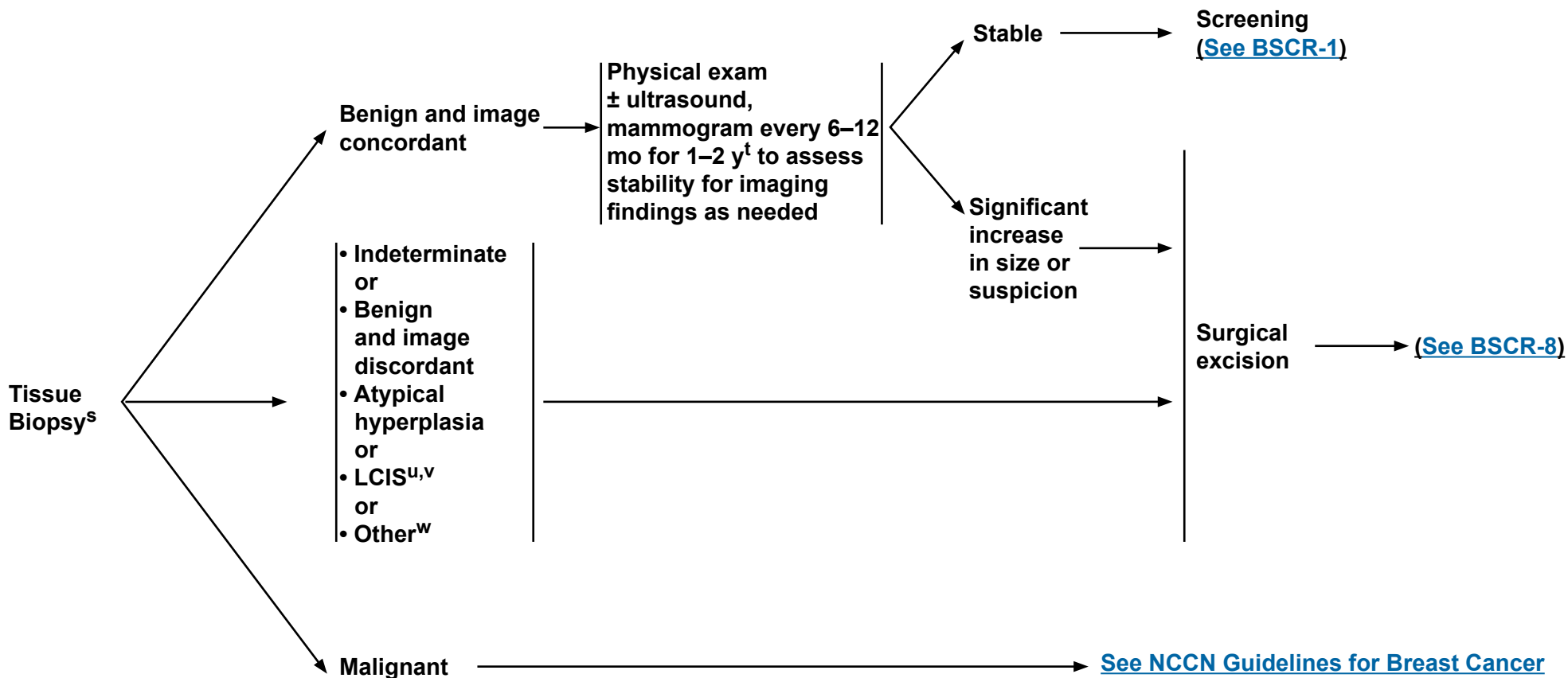


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Breast Cancer Screening and Diagnosis

PALPABLE MASS

FOLLOW-UP EVALUATION



^sFNA and core (needle or vacuum-assisted) biopsy are both valuable. FNA requires cytologic expertise. Surgical excision is appropriate if unable to perform core needle biopsy or if strongly desired by patient.

[†]There may be variability on the follow-up interval based on the level of suspicion.

^uSelect patients may be suitable for monitoring in lieu of surgical excision (eg, ALH, LCIS, papillomas, fibroepithelial lesions, radial scars).

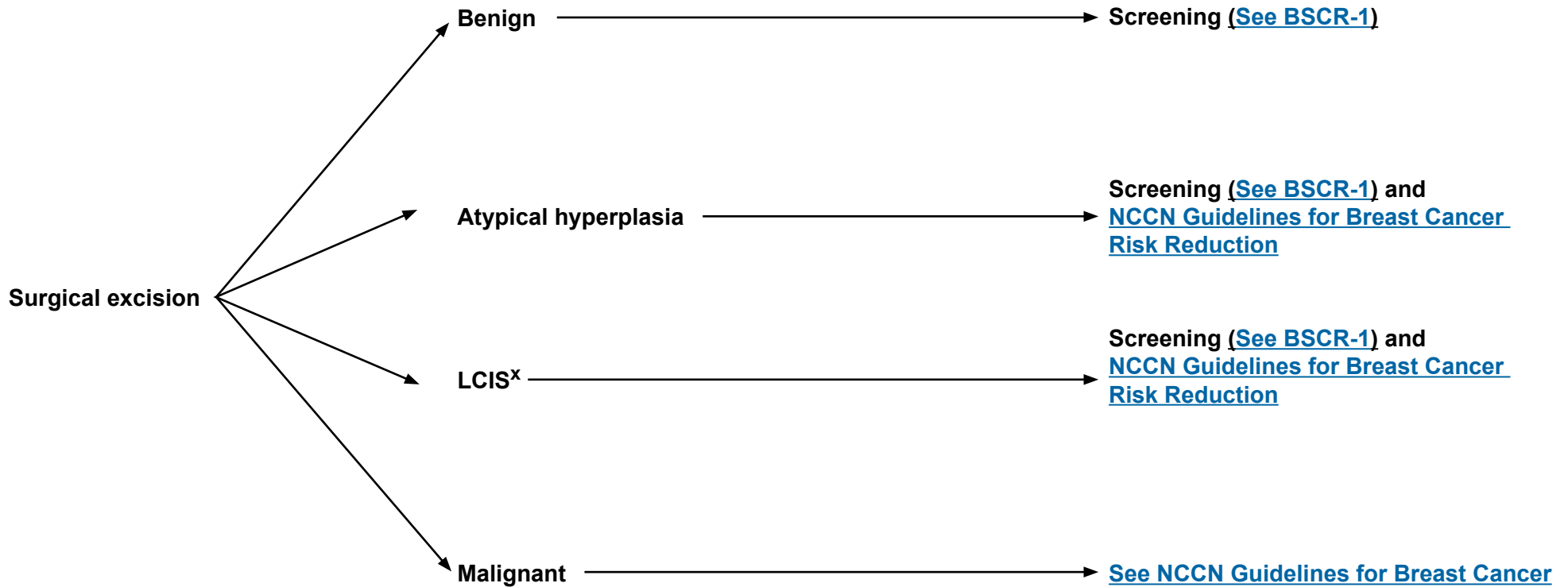
^vMultifocal/extensive LCIS involving >4 terminal ductal lobular units on a core biopsy may be associated with increased risk for invasive cancer on surgical excision.

^wOther histologies that may require additional tissue: mucin-producing lesions, potential phyllodes tumor, papillary lesions, radial scar, or histologies of concern to pathologist.

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FOLLOW-UP EVALUATION



^xPleomorphic LCIS should be managed according to the NCCN Guidelines for Breast Cancer.

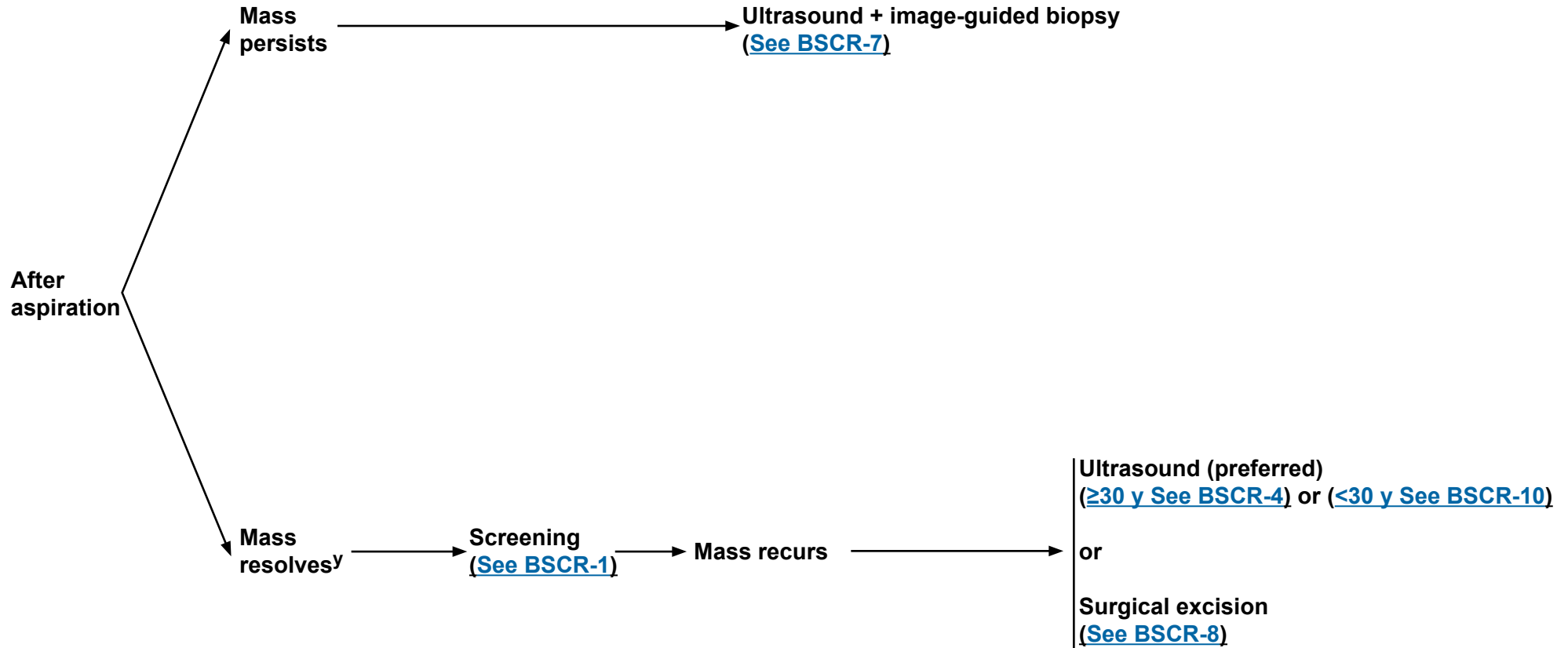
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NCCN Guidelines Version 1.2015 Breast Cancer Screening and Diagnosis

ASPIRATE FINDINGS/PALPABLE MASS

FOLLOW-UP EVALUATION



^yRoutine cytology is not recommended.

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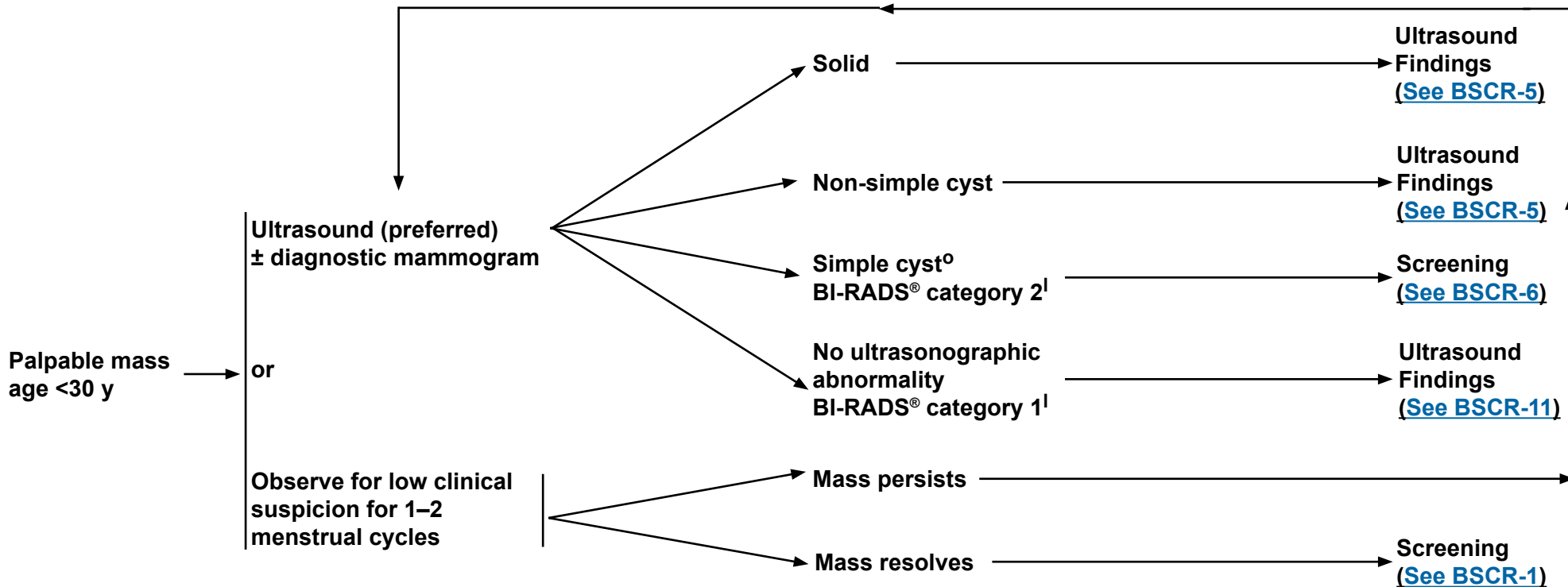


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Breast Cancer Screening and Diagnosis

PRESENTING SIGNS/SYMPTOMS

DIAGNOSTIC EVALUATION



¹See Assessment Category Definitions (BSCR-C).

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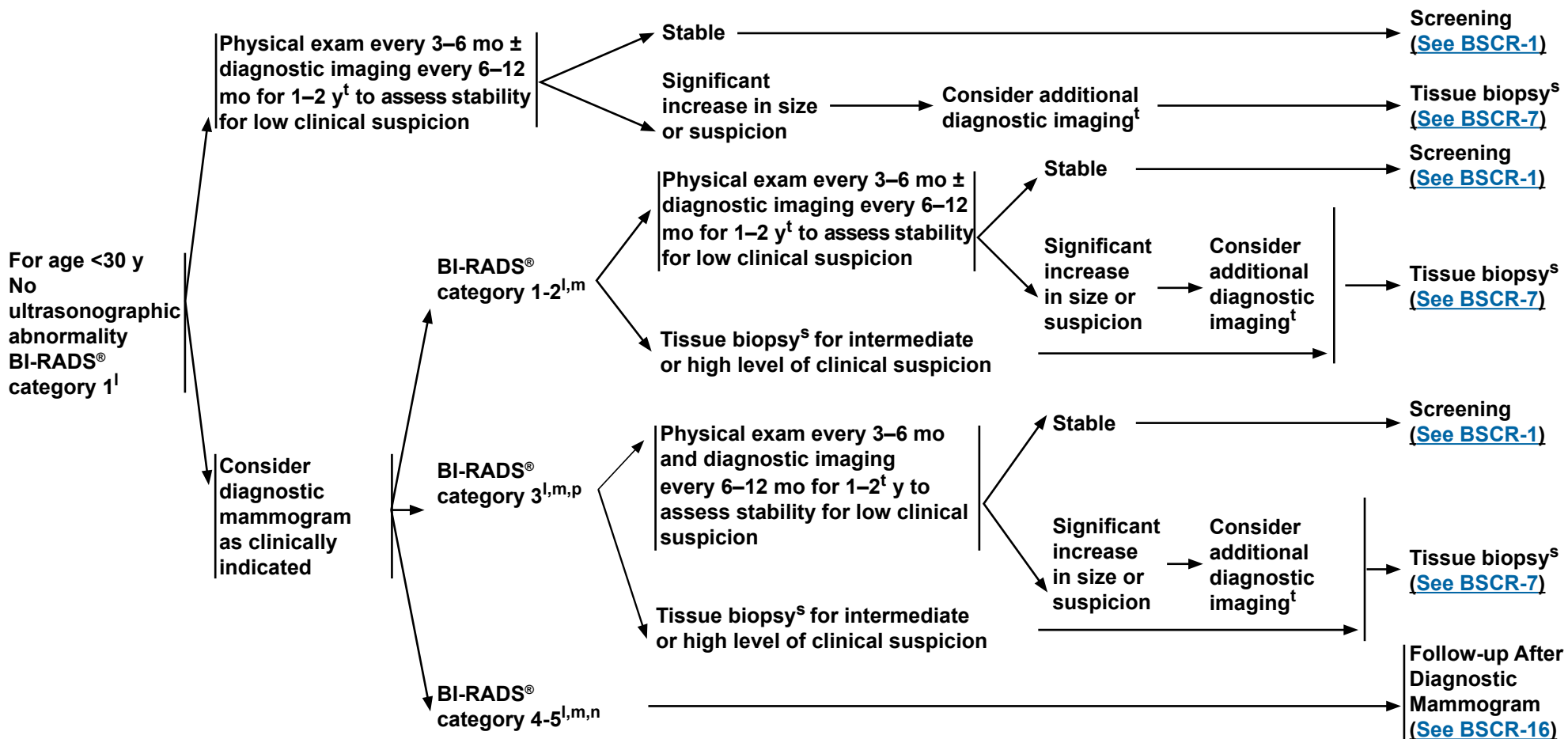


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Breast Cancer Screening and Diagnosis

ULTRASOUND FINDINGS/PALPABLE MASS

FOLLOW-UP EVALUATION



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^tThere may be variability on the follow-up interval based on the level of suspicion.

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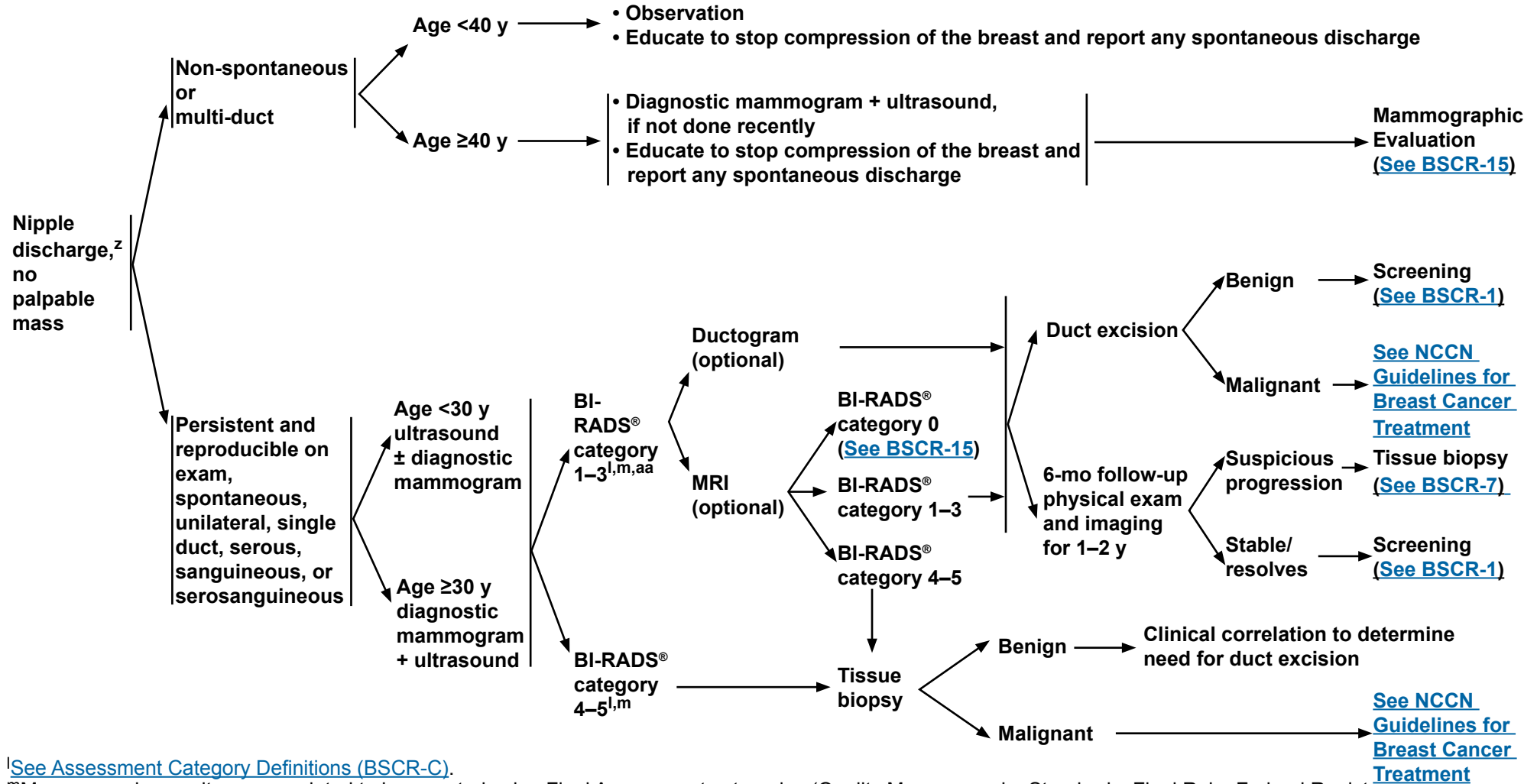
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NCCN Guidelines Version 1.2015 Breast Cancer Screening and Diagnosis

PRESENTING SIGNS/ SYMPTOMS

DIAGNOSTIC FOLLOW-UP



^lSee Assessment Category Definitions (BSCR-C).

^mMammography results are mandated to be reported using Final Assessment categories (Quality Mammography Standards: Final Rule. Federal Register. 1997;62:55988).

^zA list of drugs that can cause nipple discharge (not all-inclusive): Psychoactive drugs, antihypertensive medications, opiates, oral contraceptives, and estrogen

^{aa}If BI-RADS Category 3 finding is unrelated to nipple discharge, manage mammographic finding by [BSCR-15](#).

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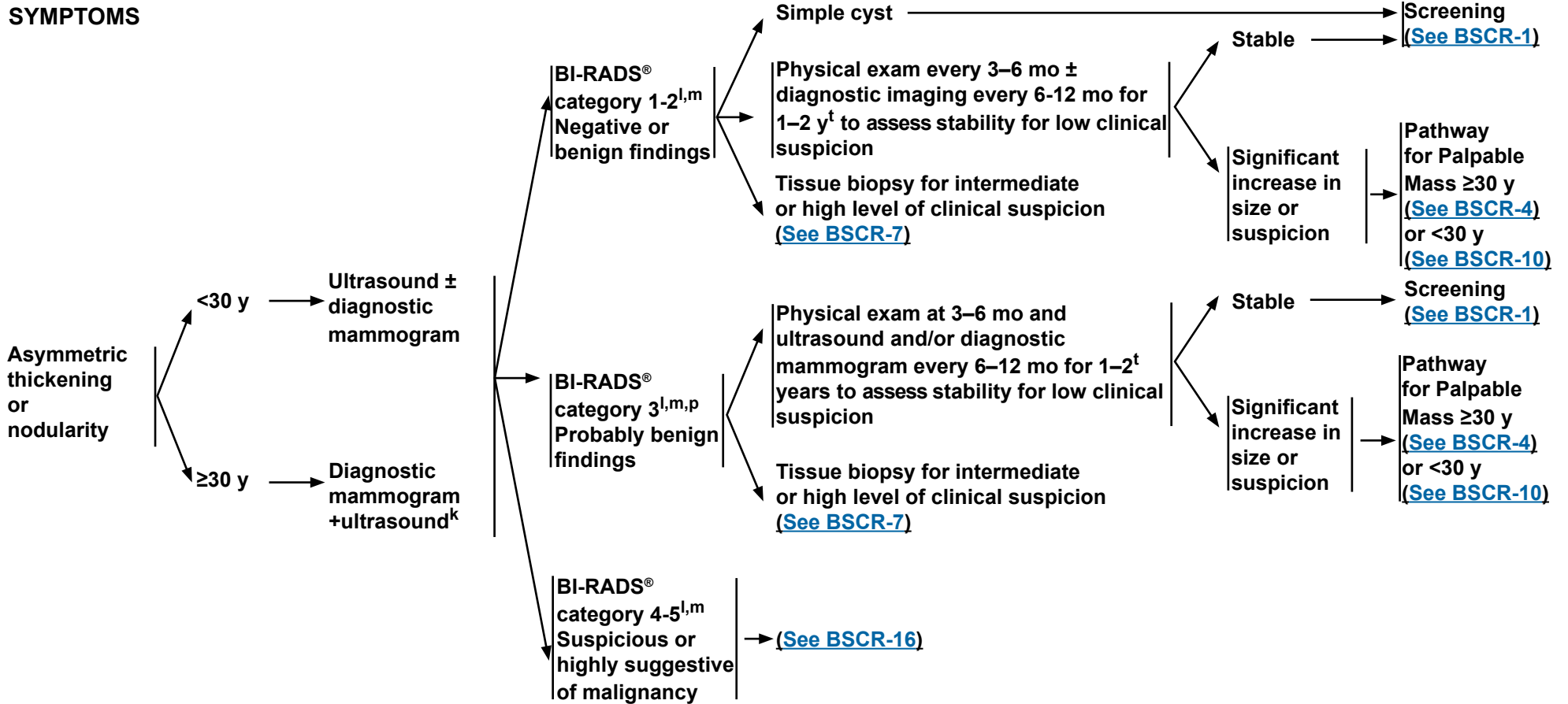


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Breast Cancer Screening and Diagnosis

PRESENTING SIGNS/ SYMPTOMS

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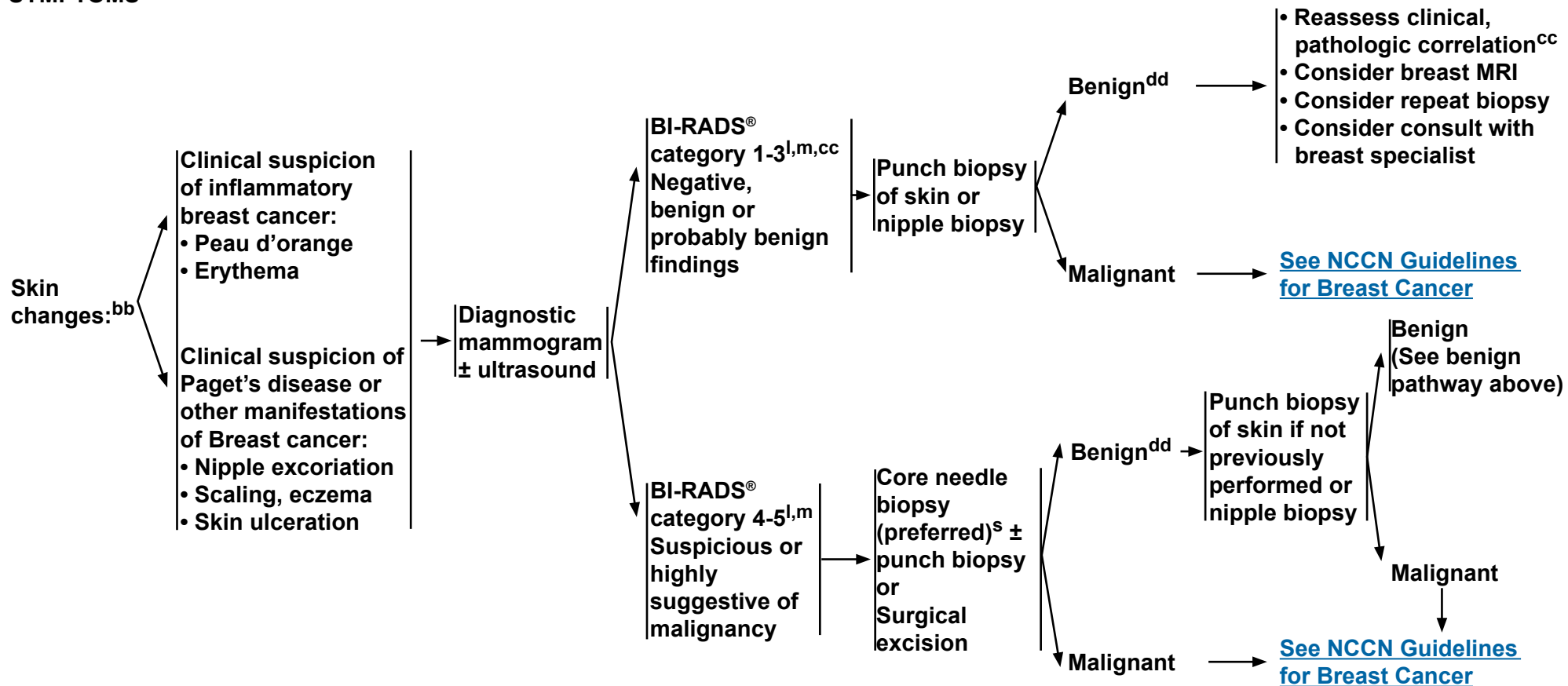


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Breast Cancer Screening and Diagnosis

PRESENTING SIGNS/ SYMPTOMS

DIAGNOSTIC FOLLOW-UP



[See Assessment Category Definitions \(BSCR-C\).](#)

^mMammography results are mandated to be reported using Final Assessment categories (Quality Mammography Standards: Final Rule. Federal Register. 1997;62:55988).

^sFNA and core (needle or vacuum-assisted) biopsy are both valuable. FNA requires cytologic expertise. Surgical excision is appropriate if unable to perform core needle biopsy or if strongly desired by patient.

^{bb}This may represent serious disease of the breast and needs evaluation.

^{cc}If clinically of low suspicion for breast cancer or high suspicion for infection, a short trial (7–10 days) of antibiotics for mastitis may be indicated.

^{dd}A benign skin punch biopsy in a patient with a clinical suspicion of inflammatory breast cancer does not rule out malignancy. Further evaluation is recommended.

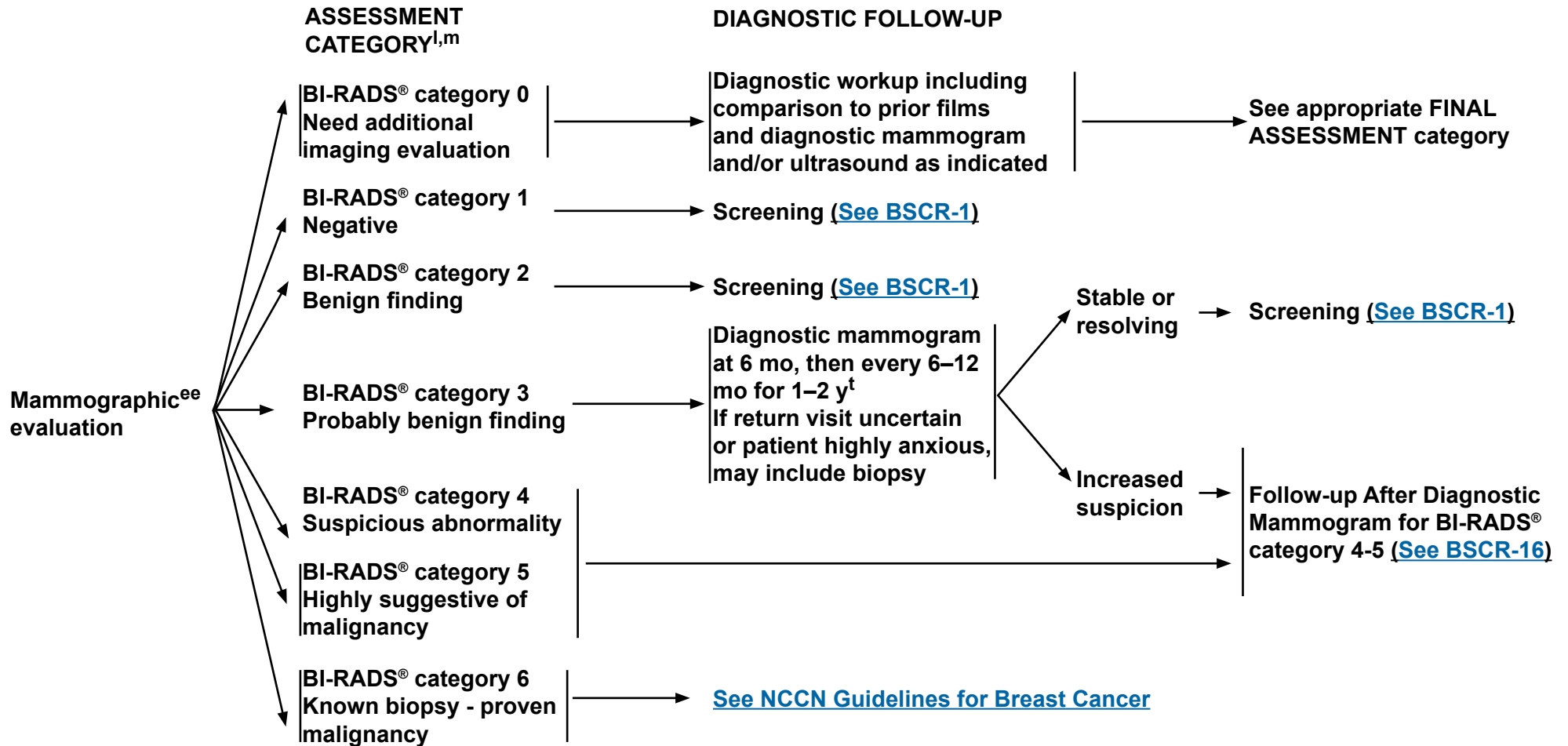
Note: All recommendations are category 2A unless otherwise indicated.

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^lSee Assessment Category Definitions (BSCR-C).

^mMammography results are mandated to be reported using Final Assessment categories (Quality Mammography Standards:Final Rule. Federal Register.1997;62:55988).

[†]There may be variability on the follow-up interval based on the level of suspicion.

^{ee}Mammogram considerations: Specify if mammogram is screening or diagnostic and comparison should be made with prior noncopied films (original films), if obtainable.

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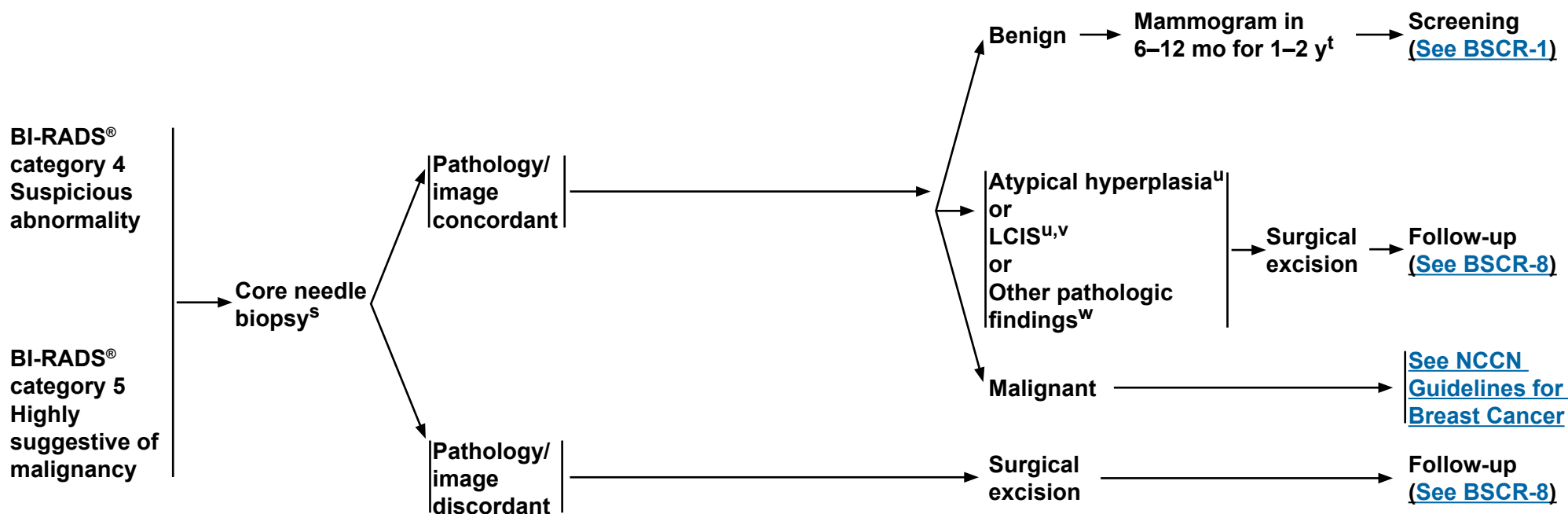


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ASSESSMENT CATEGORY^{l,m}

FOLLOW-UP AFTER DIAGNOSTIC IMAGING



^lSee Assessment Category Definitions (BSCR-C).

^mMammography results are mandated to be reported using Final Assessment categories (Quality Mammography Standards: Final Rule. Federal Register. 1997;62:55988).

^sFNA and core (needle or vacuum-assisted) biopsy are both valuable. FNA requires cytologic expertise. Surgical excision is appropriate if unable to perform core needle biopsy.

^tThere may be variability on the follow-up interval based on the level of suspicion.

^uSelect patients may be suitable for monitoring in lieu of surgical excision (eg, ALH, LCIS, papillomas, fibroepithelial lesions, radial scars).

^vMultifocal/extensive LCIS involving >4 terminal ductal lobular units on a core biopsy may be associated with increased risk of invasive cancer on surgical excision

^wOther histologies that may require additional tissue: mucin-producing lesions, potential phyllodes tumor, papillary lesions, radial scar, or histologies of concern to pathologist.

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Breast Cancer Screening and Diagnosis

BREAST SCREENING CONSIDERATIONS

- **Women should be counseled regarding potential benefits, risks, and limitations of breast screening.**
- **Adequate clinical breast exams include the following: upright and supine position during inspection, palpation of all components of the breast, axilla, and clavicular lymph node basins. Time spent on the palpable portion of the exam is associated with increased detection of palpable abnormalities. O'clock location and distance from nipple facilitate geographic correlation with imaging findings.**
- **Consider severe comorbid conditions limiting life expectancy and whether therapeutic interventions are planned.**
- **Upper age limit for screening is not yet established.**
- **Dense breasts limit the sensitivity of mammography. Dense breasts are associated with an increased risk for breast cancer, but there is insufficient evidence to support routine supplemental screening in women with dense breasts and no other risk factors. Important outcomes are not yet established for supplemental screening; some states have passed legislation mandating patient notification of breast density.**
- **There are several studies supporting the use of supplemental screening for breast cancer as an adjunct to screening mammography for women with dense breast tissue. Different modalities may be considered based on risk.¹**
- **Digital mammography appears to benefit young women and women with dense breasts.²**
- **Early studies show promise for tomosynthesis mammography. Several studies show a combined use of digital mammography and tomosynthesis resulted in improved cancer detection and decreased call back rates. Of note, most studies used double the dose of radiation. The radiation dose can be minimized by synthetic 2-D reconstruction. Definitive studies are still pending.**
- **Current evidence does not support the routine use of breast scintigraphy (eg, sestamibi scan) or ductal lavage as screening procedures**

¹Berg WA, Blume JD, Cormack JB, et al. Combined screening with ultrasound and mammography vs. mammography alone in women at elevated risk of breast cancer. JAMA 2008;299(18):2151-2163.

²Pisano ED, Gatsonis C, Hendrick E et al for the Digital Mammographic Imaging Screening Trial (DMIST) Investigators. Diagnostic performance of digital versus film mammography for breast cancer screening. N Engl J Med 2005;353:1773-1783.

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BREAST SCREENING CONSIDERATIONS

RECOMMENDATIONS FOR BREAST MRI SCREENING AS AN ADJUNCT TO MAMMOGRAPHY^{3,4} (FOR AGE TO BEGIN SCREENING EXCEPT WHERE NOTED BELOW: [SEE BSCR-2](#))

Recommend Annual MRI Screening (Based on Evidence):⁵

- *BRCA* mutation, commence at age 25 y
- First-degree relative of *BRCA* carrier, but untested: commence at age 25 y
- Lifetime risk 20% or greater, as defined by models that are largely dependent on family history⁶

Recommend Annual MRI Screening (Based on Expert Consensus Opinion):⁷

- Radiation to chest between age 10 and 30 years
- Li-Fraumeni syndrome⁷ and first-degree relatives
- Cowden and Bannayan-Riley-Ruvalcaba syndromes⁸ and first-degree relatives
- Consider MRI screening for LCIS and ALH/ADH based on emerging evidence

Insufficient Evidence to Recommend for or Against MRI Screening:⁹

- Lifetime risk 15%–20%, as defined by models that are largely dependent on family history⁶
- Heterogeneously or extremely dense breast on mammography
- Women with a personal history of breast cancer,¹⁰ including ductal carcinoma in situ (DCIS)

Recommend Against MRI Screening (Based on Expert Consensus Opinion):

- Women at <15% lifetime risk

³Adapted with permission from John Wiley and Sons. Copyright ©2007 American Cancer Society. Saslow D, Boetes C, Burke W, et al. American Cancer Society Guidelines for Breast Cancer Screening with MRI as an Adjunct to Mammography. CA: Cancer J Clin 2007;57:75-89.

⁴Breast MRI examinations require a dedicated breast coil and breast imaging radiologists familiar with the optimal timing sequences and other technical details for image interpretation. The imaging center should have the ability to perform MRI-guided needle sampling and/or wire localization of MRI-detected findings.

⁵Evidence from nonrandomized screening trials and observational studies.

⁶Risk models that are largely dependent on family history (eg, Claus, BRCAPRO, BOADICEA, Tyrer-Cuzick). [See NCCN Guidelines for Breast Cancer Risk Reduction.](#)

⁷Based on evidence of lifetime risk for breast cancer.

⁸There is variation in recommendations for initiation of screening for different genetic syndromes. [See NCCN Guidelines for Genetic/Familial High-Risk Assessment:Breast and Ovarian.](#)

⁹Payment should not be a barrier. Screening decisions should be made on a case-by-case basis, as there may be particular factors to support MRI. More data on these groups is expected to be published soon.

¹⁰Brennan S, Liberman L, Dershaw DD, et al. Breast MRI screening of women with a personal history of breast cancer. AJR 2010;195:510-516.

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RISK FACTORS USED IN THE MODIFIED GAIL MODEL, AGE ≥35 Years¹

- Current age
- Age at menarche
- Age at first live birth or nulliparity
- Number of first-degree relatives with breast cancer
- Number of previous benign breast biopsies
- Atypical hyperplasia in a previous breast biopsy
- Race²

For calculation of risk, based on the modified Gail Model, see <http://www.cancer.gov/bcrisktool/Default.aspx>

¹For detailed information, see <http://www.cancer.gov/bcrisktool/Default.aspx>.

²The current Gail Model may not accurately assess breast cancer risk in non-Caucasian women.

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Breast Cancer Screening and Diagnosis

MAMMOGRAPHIC ASSESSMENT CATEGORY DEFINITIONS^{1,2}

BI-RADS® - MAMMOGRAPHY FINDINGS

A. Assessment Is Incomplete:

Category 0: Incomplete - Need Additional Imaging Evaluation and/or Prior Mammograms for Comparison:

There is a finding for which additional evaluation is needed. This is almost always used in a screening situation. Under certain circumstances this assessment category may be used in a diagnostic mammography report, such as when ultrasound equipment or personnel are not immediately available, or when the patient is unable or unwilling to wait for completion of a full diagnostic examination. A recommendation for additional imaging evaluation includes the use of spot compression (with or without magnification), special mammographic views, and ultrasound. Category 0 should not be used for diagnostic breast imaging findings that warrant further evaluation with MRI. Rather, the interpreting physician should issue a final assessment in a report that is made before the MRI examination is performed. In most circumstances and when feasible, if a mammography examination is not assessed as negative or benign, the current examination should be compared with prior examination(s). The interpreting physician should use judgment on how vigorously to attempt obtaining prior examinations, given the likelihood of success of such an endeavor and the likelihood that comparison will affect the final assessment. In this context, it is important to note that comparison with previous examination(s) may be irrelevant when a finding is inherently suspicious for malignancy.

Category 0 should be used for prior image comparison only when such comparison is required to make a final assessment. When category 0 is used in the context of awaiting prior examinations for comparison, there should be in place a tracking procedure guaranteeing with 100% reliability that a final assessment will be made within 30 days (preferably sooner) even if prior examinations do not become available. Some mammography practices may reasonably choose never to use category 0 in the context of awaiting prior examinations simply because they do not have a 100% reliable tracking procedure. If a mammography examination is assessed as category 0 in the context of awaiting prior examinations and then the prior examinations do become available, an addendum to the initial mammography report should be issued, including a revised assessment. For auditing purposes, the revised assessment should replace the initial assessment.

¹Mammography results are mandated to be reported using Final Assessment categories (Quality Mammography Standards: Final Rule. Federal Register. 1997;62:55988).

²Terminology in this table is reflective of the American College of Radiology (ACR). ACR-BI-RADS®--5th Edition. ACR Breast Imaging Reporting and Data System, Breast Imaging Atlas; BI-RADS. Reston VA. American College of Radiology, 2014. For more information, see www.acr.org. Reprinted with permission from the American College of Radiology. No other representation of this document is authorized without express, written permission from the American College of Radiology.

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Breast Cancer Screening and Diagnosis

MAMMOGRAPHIC ASSESSMENT CATEGORY DEFINITIONS^{1,2}

BI-RADS® - MAMMOGRAPHY FINDINGS

B. Assessment Is Complete - Final Assessment Categories:

Category 1: Negative:

There is nothing to comment on. This is a normal examination.

Category 2: Benign:

Like Category 1, this is a "normal" assessment, but here, the interpreter chooses to describe a benign finding in the mammography report. Involuting, calcified fibroadenomas, skin calcifications, metallic foreign bodies (such as core biopsy and surgical clips), and fat-containing lesions (such as oil cysts, lipomas, galactoceles, and mixed-density hamartomas) all have characteristically benign appearances and may be described with confidence. The interpreter may also choose to describe intramammary lymph nodes, vascular calcifications, implants, or architectural distortion clearly related to prior surgery while still concluding that there is no mammographic evidence of malignancy. On the other hand, the interpreter may choose not to describe such findings, in which case the examination should be assessed as negative (category 1).

Note that both category 1 and category 2 assessments indicate that there is no mammographic evidence of malignancy. Both should be followed by the management recommendation for routine mammography screening. The difference is that category 2 should be used when describing one or more specific benign mammographic findings in the report, whereas category 1 should be used when no such findings are described (even if such findings are present).

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Breast Cancer Screening and Diagnosis

MAMMOGRAPHIC ASSESSMENT CATEGORY DEFINITIONS^{1,2}

BI-RADS® - MAMMOGRAPHY FINDINGS

Category 3: Probably Benign:

A finding assessed using this category should have a $\leq 2\%$ likelihood of malignancy, but greater than the essentially 0% likelihood of malignancy of a characteristically benign finding. A probably benign finding is not expected to change over the suggested period of imaging surveillance, but the interpreting physician prefers to establish stability of the finding before recommending management limited to routine mammography screening.

There are several prospective clinical studies demonstrating the safety and efficacy of periodic mammographic surveillance instead of biopsy for specific mammographic findings.

Three specific findings are validated as being probably benign (the noncalcified circumscribed solid mass, the focal asymmetry, and solitary group of punctate calcifications). All the previously cited studies emphasize the need to conduct a complete diagnostic imaging evaluation before making a probably benign (category 3) assessment; hence, it is recommended not to render such an assessment in interpreting a screening mammography examination. The practice of rendering category 3 assessments directly from screening examination also has been shown to result in adverse outcomes: 1) unnecessary follow-up of many lesions that could have been promptly assessed as benign; and 2) delayed diagnosis of a small number of cancers that otherwise may have been smaller in size and less likely to be advanced in stage. Also, all the previously cited studies exclude palpable lesions, so the use of a probably benign assessment for a palpable lesion is not supported by robust scientific data, although there are two single-institution studies that do report successful outcomes for palpable lesions. Finally, because evidence from previously cited studies indicates the need for biopsy rather than continued surveillance when a probably benign finding increases in size or extent, it is not prudent to render a category 3 assessment when a finding that otherwise meets “probably benign” imaging criteria is either new or has increased in size or extent.

While the vast majority of probably benign findings are managed with an initial short-interval follow-up (6-mo) examination followed by additional examinations until long-term (2- or 3-year) stability is demonstrated, there may be occasions in which a biopsy is done instead (patient preference or overriding clinical concern).

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Breast Cancer Screening and Diagnosis

MAMMOGRAPHIC ASSESSMENT CATEGORY DEFINITIONS^{1,2}

BI-RADS® - MAMMOGRAPHY FINDINGS

Category 4: Suspicious:

This category is reserved for findings that do not have the classic appearance of malignancy but are sufficiently suspicious to justify a recommendation for biopsy. The ceiling for category 3 assessment is a 2% likelihood of malignancy and the floor for category 5 assessment is 95%, so category 4 assessments cover the wide range of likelihood of malignancy in between. Thus, almost all recommendations of breast interventional procedures will come from assessments made using this category. By subdividing category 4³ into 4A, 4B, and 4C, as recommended in Guidance chapter and using the cut point indicated therein, it is hoped that patients and referring clinicians will more readily make informed decisions on the ultimate course of action.

Category 5: Highly Suggestive of Malignancy:

These assessments carry a very high probability (≥95%) of malignancy. This category initially was established to involve lesions for which 1-stage surgical treatment was considered without preliminary biopsy, in an era when preoperative wire localization was the primary breast interventional procedure. Nowadays, given the widespread acceptance of imaging-guided percutaneous biopsy, 1-stage surgery is rarely, if ever, performed. Rather, current oncologic management almost always involves tissue diagnosis of malignancy via percutaneous tissue sampling to facilitate treatment options, such as when sentinel node biopsy is included in surgical management or when neoadjuvant chemotherapy is administered prior to surgery. Therefore, the current rationale for using a category 5 assessment is to identify lesions for which any non-malignant percutaneous tissue diagnosis is automatically considered discordant, resulting in the recommendation for repeat (usually surgical) biopsy.

Category 6: Known Biopsy - Proven Malignancy:

This category is reserved for examinations performed after biopsy proof of malignancy (imaging performed after percutaneous biopsy but prior to complete surgical excision) in which there are no mammographic abnormalities other than the known cancer that might need additional evaluation.

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³The new BI-RADS® cut points for the risk of malignancy are as follows: 4A (>2% - ≤10%), 4B (>10% - ≤50%), 4C (>50% - <95%).

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Breast Cancer Screening and Diagnosis

ULTRASOUND ASSESSMENT CATEGORY DEFINITIONS^{1,2}

BI-RADS® - ULTRASOUND FINDINGS

A. Assessment is Incomplete:

Category 0: Incomplete - Need Additional Imaging Evaluation:

There is a finding for which additional imaging evaluation is needed. This is almost always used in a screening situation. In this context, additional imaging evaluation includes the recording of (nonstandard) ultrasound images to supplement the standard images recorded for a screening examination. Note that this does not include repeat real-time scanning by the interpreting physician and/or colleague as long as additional images are not recorded. This respects the unique real-time nature of ultrasound and does not penalize its use.

Under certain circumstances, assessment category 0 may be used in a diagnostic ultrasound report, such as when equipment or personnel are not immediately available to perform a needed concurrent diagnostic mammography examination, or when the patient is unable or unwilling to wait for completion of a full diagnostic examination. Category 0 should not be used for diagnostic breast imaging findings that warrant further evaluation with MRI. Rather, the interpreting physician should issue a final assessment in a report that is made before the MRI examination is performed.

In most circumstances and when feasible, if a screening ultrasound examination is not assessed as negative or benign, the current examination should be compared to prior examination(s), if any exist. The interpreting physician should use judgment on how vigorously to attempt obtaining prior examinations, given the likelihood of success of such an endeavor and the likelihood that comparison will affect the final assessment. In this context, it is important to note that comparison to previous examination(s) may be irrelevant when a finding is inherently suspicious for malignancy.

Category 0 should be used for prior image comparison only when such comparison is required to make a final assessment. When category 0 is used in the context of awaiting prior examinations for comparison, there should be in place a tracking system guaranteeing with 100% reliability that a final assessment will be made within 30 days (preferably sooner), even if prior examinations do not become available. Some breast imaging practices may reasonably choose never to use category 0 in the context of awaiting prior examinations simply because they do not have a 100% reliable tracking system. If an ultrasound examination is assessed as category 0 in the context of awaiting prior examinations and then the prior examinations do become available, an addendum to the initial ultrasound report should be issued, including a revised assessment. For auditing purposes, the revised assessment should replace the initial assessment.

A need for previous studies to determine appropriate management might also temporarily defer a final assessment.

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ULTRASOUND ASSESSMENT CATEGORY DEFINITIONS^{1,2}

BI-RADS® - ULTRASOUND FINDINGS

B. Assessment is Complete — Final Categories:

Category 1: Negative:

There is nothing to comment on. This is a normal examination.

Category 2: Benign:

As with category 1, this is a “normal” assessment, but here the interpreter chooses to describe a benign finding in the ultrasound report. For example, the interpreter may choose to describe one or more simple cysts, intramammary lymph nodes, postsurgical fluid collections, breast implants, or complicated cysts/probable fibroadenomas that are unchanged for at least 2 or 3 years, while still concluding that there is no sonographic evidence of malignancy. On the other hand, the interpreter may choose not to describe such findings, in which case the examination should be assessed as negative (category 1).

Note that both category 1 and category 2 assessments indicate that there is no sonographic evidence of malignancy. Both should be followed by the management recommendation for routine age-appropriate screening. The difference is that category 2 should be used when describing one or more specific benign sonographic findings in the report, whereas category 1 should be used when no such findings are described (even if such findings are present).

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Breast Cancer Screening and Diagnosis

ULTRASOUND ASSESSMENT CATEGORY DEFINITIONS^{1,2}

BI-RADS® - ULTRASOUND FINDINGS

Category 3: Probably Benign:

Assessment category 3, probably benign, is not an indeterminate category for use simply when the radiologist is unsure whether to render a benign (BI-RADS® category 2) or suspicious (BI-RADS® category 4) assessment, but is one that is reserved for specific imaging findings known to have >0% but ≤2% likelihood of malignancy. For ultrasound, there is robust evidence that a solid mass with a circumscribed margin, oval shape, and parallel orientation (most commonly fibroadenoma) and an isolated complicated cyst have a likelihood of malignancy in the defined (≤2%), probably benign range, for which short-interval (6-month) follow-up sonography and then periodic sonographic surveillance may represent appropriate management. Similar data have been reported for clustered microcysts, but these data are less strong because they involve much fewer cases. The use of assessment category 3 for sonographic findings other than these three should be considered only if the radiologist has personal experience to justify a watchful-waiting approach, preferably involving observation of a sufficient number of cases of an additional sonographic finding to suggest a likelihood of malignancy within the defined (≤2%), probably benign range.

This edition of the BI-RADS® Atlas also emphasizes the recommendation that a category 3 assessment should not be made at screening; rather, this should be done only after completion of full diagnostic breast imaging examination. This recommendation is appropriate for screening mammography, for which batch interpretation usually is utilized, because in this setting there is no opportunity to complete the diagnostic workup before interpreting the screening examination. However, screening ultrasound almost always is interpreted online, so a full diagnostic examination also is completed while the patient remains in the breast imaging facility, and a single breast imaging report may be issued that combines the findings of both screening and diagnostic components of the examination. Hence, there is no purpose in recommending against category 3 assessment at screening ultrasound, because the diagnostic workup would be completed simultaneously. Note that for auditing purposes, the screening component of a category 3-assessed screening ultrasound examination will be audit-positive, not only because additional nonstandard (diagnostic) images will be recorded but also because a category 3 assessment at screening is defined as being audit-positive.

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Breast Cancer Screening and Diagnosis

ULTRASOUND ASSESSMENT CATEGORY DEFINITIONS^{1,2}

BI-RADS® - ULTRASOUND FINDINGS

For category 3 assessments, the initial short-term follow-up interval is usually 6 months and involves the breast(s) containing the probably benign finding(s). Assuming stability at this 6-month examination, a category 3 assessment again is rendered with a management recommendation for a second short-interval follow-up examination in 6 months. Again assuming stability at this second short-interval follow-up, the examination is once more assessed as category 3, but now the recommended follow-up interval usually is lengthened to 1 year due to the already-observed 12-month stability. Note that although the 1-year follow-up coincides with the routine screening interval in the United States, a category 3 assessment is rendered to indicate that the period of imaging surveillance is still underway. As with surveillance using mammography, after 2 to 3 years of stability, the final assessment category should be changed to benign (BI-RADS® category 2). A benign evaluation may also be rendered before completion of category 3 analysis if, in the opinion of the interpreter, the finding has no chance of malignancy and is thus a category 2.

Category 4: Suspicious:

This category is reserved for findings that do not have the classic appearance of malignancy but are sufficiently suspicious to justify a recommendation for biopsy. The ceiling for category 3 assessment is a 2% likelihood of malignancy, and the floor for category 5 assessment is 95%, so category 4 assessments cover the wide range of likelihood of malignancy in between. Thus, almost all recommendations for breast interventional procedures will come from assessments made using this category. By subdividing category 4³ into 4A, 4B, and 4C, it is hoped that patients and referring clinicians will more readily make informed decisions on the ultimate course of action. An example of separating the BI-RADS® assessment category from the management recommendation occurs when a simple cyst, correctly assessed as BI-RADS® 2, undergoes cyst aspiration for pain control.

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³The new BI-RADS® cut points for the risk of malignancy are as follows: 4A (>2% - ≤10%), 4B (>10% - ≤50%), 4C (>50% - <95%).

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**ULTRASOUND ASSESSMENT CATEGORY DEFINITIONS^{1,2}****BI-RADS® - ULTRASOUND FINDINGS****Category 5: Highly Suggestive of Malignancy:**

These assessments carry a very high probability (≥95%) of malignancy. This category initially was established to involve lesions for which 1-stage surgical treatment could be considered without preliminary biopsy in an era when preoperative wire localization was the primary breast interventional procedure. Nowadays, given the widespread acceptance of imaging-guided percutaneous biopsy, 1-stage surgery rarely, if ever, is performed. Rather, current oncologic management almost always involves tissue diagnosis of malignancy via percutaneous tissue sampling to facilitate treatment options, such as when sentinel node imaging is included in surgical management or when neoadjuvant chemotherapy is administered prior to surgery. Therefore, the current rationale for using a category 5 assessment is to identify lesions for which any nonmalignant percutaneous tissue diagnosis is considered discordant, resulting in the recommendation for repeat (usually vacuum-assisted or surgical) biopsy. Also note that whereas the fourth edition simply indicated that “appropriate action should be taken” as management for category 5 assessments, the fifth edition provides the more directed management recommendation that “biopsy should be performed in the absence of clinical contraindication.” This new text unequivocally specifies tissue diagnosis as the interpreting physician’s management recommendation for category 5 assessments, appropriately and effectively transferring the burden of establishing a contraindication to this recommendation to the referring clinician.

Category 6: Known Biopsy-Proven Malignancy:

This category is reserved for examinations performed after biopsy proof of malignancy (imaging performed after percutaneous biopsy but prior to surgical excision), in which there are no abnormalities other than the known cancer that might need additional evaluation.

¹Mammography results are mandated to be reported using Final Assessment categories (Quality Mammography Standards: Final Rule. Federal Register. 1997;62:55988).

²Terminology in this table is reflective of the American College of Radiology (ACR). ACR-BI-RADS®--5th Edition. ACR Breast Imaging Reporting and Data System, Breast Imaging Atlas; BI-RADS. Reston VA. American College of Radiology, 2014. For more information, see www.acr.org. Reprinted with permission from the American College of Radiology. No other representation of this document is authorized without express, written permission from the American College of Radiology.

Note: All recommendations are category 2A unless otherwise indicated.

Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

Discussion

This discussion is being updated to correspond with the newly updated algorithm. Last updated 07/03/14

NCCN Categories of Evidence and Consensus

Category 1: Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

Category 2A: Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

Category 2B: Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.

Category 3: Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

All recommendations are category 2A unless otherwise noted.

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Overview

The average lifetime risk of breast cancer for a woman in the United States has been estimated at 12.3% (ie, 1 in 8 women).¹ In 2013, the American Cancer Society (ACS) estimates, 64,640 cases of female carcinoma in situ of the breast and 234,580 cases of invasive breast cancer (232,340 women and 2240 men) will be diagnosed in the United States.² About 40,030 deaths are estimated in 2013.² The good news is that mortality from breast cancer has dropped slightly. This decrease has, in part, been attributed to mammographic screening.³

The National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology® (NCCN Guidelines®) for Breast Cancer Screening and Diagnosis are for facilitating clinical decision-making. The general public and health care providers need to be aware that mammography or any other imaging modality is not a stand-alone procedure. Neither the current technology of mammography or other imaging tests nor the subsequent interpretation of such tests is foolproof. Clinical judgment is needed to ensure appropriate management. The patient's concerns and physical findings must be taken into account along with imaging results and histologic assessment.

Breast Screening

Breast screening is performed in women without any signs or symptoms of breast cancer so that disease can be detected as early as possible. The components of a breast screening evaluation are dependent on patient age and other factors such as medical and family history, and can include breast awareness (ie, patient familiarity with her breasts), physical examination, risk assessment, screening mammography, and in selected cases, screening breast magnetic resonance imaging (MRI).

A diagnostic breast evaluation differs from breast screening in that it is used to evaluate an existing problem (eg, palpable mass, discharge from the nipple). Although there is preliminary evidence that breast ultrasonography can be a useful screening adjunct to mammography in the evaluation of high-risk women with dense breasts,⁴ its use as a screening test is not recommended at this time. These guidelines include ultrasonography in the diagnostic work-up of selected women only based on specific positive findings (see section on “Breast Ultrasonography” on MS-12). Current evidence does not support the routine use of breast scintigraphy (eg, sestamibi scan) or ductal lavage as screening procedures.

History and physical examination

The starting point of these guidelines for screening and evaluating breast abnormalities is a complete medical history followed by the clinical breast examination (CBE). Inspection of the breasts should be performed with the patient in upright and supine positions. Positioning may be done so as to elicit any subtle shape or contour changes in the breast.⁵

Women should be familiar with their breasts and promptly report any change to their health care provider.^{6,7} This does not need to be in any specific formalized education program. Data from a large randomized trial of breast self-examination (BSE) screening has shown that instruction in BSE has no effect on reducing breast cancer mortality. In this study, 266,064 women were randomly assigned to either receive instruction in BSE or not.⁸ Compliance was encouraged through feedback and reinforcement sessions. After 10 to 11 years of follow-up, 135 breast cancer deaths in the instruction group and 131 in the control group were observed and the cumulative breast cancer mortality rates were not significantly different between the two arms (RR, 1.04; 95% CI,

0.82–1.33; $P = .72$). The number of benign breast lesions detected in the BSE instruction group was higher than that detected in the control group. Nevertheless, women should be encouraged to be aware of their breasts since this may facilitate detection of interval cancers between routine screenings. The NCCN Panel recommends that the women should be familiar with their breasts and promptly report changes to their health care provider and that periodic, consistent BSE may facilitate breast self-awareness.

Risk Assessment

If the physical examination is negative in an asymptomatic woman, the next decision point is based on risk stratification. Women can be stratified into two basic categories for the purpose of screening recommendations: those at average risk and those at increased risk. Risk assessment is outlined in the [NCCN Guidelines for Breast Cancer Risk Reduction](#). The increased risk category consists of six groups: (1) women with a prior history of breast cancer; (2) women 35 years or older with a 5-year risk of invasive breast carcinoma $\geq 1.7\%$ by per Gail model; (3) women with a lifetime risk of breast cancer $> 20\%$ based on models largely dependent on family history; (4) women who have previously received therapeutic thoracic irradiation (eg. mantle irradiation) between the ages of 10-30 years; (5) women with lobular carcinoma in situ (LCIS) and (6) women with a pedigree suggestive of or with a known genetic predisposition.

Screening Women at Average Risk

For women between ages 25 and under 40 years, the NCCN Panel recommends CBE every 1 to 3 years and breast awareness encouraged.

For women aged 40 years and older, the NCCN Panel recommends annual CBE and screening mammography, and encourages breast awareness. Although controversies persist regarding the benefits and risks of mammographic screening in certain age groups (notably women age 40-49),⁹⁻¹⁶ most medical experts reaffirmed current recommendations supporting screening mammography (see section on “Mammographic Evaluation” on MS-8). The recommendation that women at normal risk begin annual mammographic screening at age 40 years is based on a consensus statement from the American Cancer Society (ACS) and National Cancer Institute in 1997 and is supported by the ACS guidelines for breast cancer screening published in 2003,¹⁵ as well as the results and meta-analyses of randomized clinical trials. Women also should be informed about the evidence demonstrating the value of detecting breast cancer early, before symptoms develop. The benefits of early detection include less aggressive treatment and a wide range of treatment options. The evaluation of benefits versus risk strongly supports the value of screening and the importance of adhering to a schedule of regular mammograms.

A second consideration is the time interval of screening in women aged 50-74 years. Whether breast screening should be performed annually or every other year remains controversial.¹⁶ The NCCN Panel believes that the benefits of yearly mammography outweigh the risks of the procedure as breast cancer mortality is lower with annual compared to biennial screening mammograms.¹⁷ Additionally, mammograms can often detect a lesion 2 years before the lesion is discovered by CBE. To reduce mortality from breast cancer, yearly screening is thought to be more beneficial.

There are limited data regarding screening of elderly women because most clinical trials for breast screening have used a cutoff age of 65 or 70 years.¹⁸⁻²⁰ With the high incidence of breast cancer in the elderly

population, the same screening guidelines used for women who are age 40 or older are recommended. Clinicians should always use judgment when applying screening guidelines. Mammography screening should be individualized weighing its potential benefits/risks in the context of the patients overall health and estimated longevity.²¹ If a patient has severe comorbid conditions limiting her life expectancy and no intervention would occur based on the screening findings, then the patient should not undergo screening.^{15,21}

Recently Bleyer and Welch published a study on screening mammography and the risk of over-diagnosis of breast cancer.²² The NCCN panel believes that this study analysis is misleading. The authors used the period 1976 through 1978 to estimate an annual increase of 0.25% in breast-cancer incidence. In fact, 40 years of recorded data shows that the actual increase is 1% per year.²³ In addition, the study analysis did not differentiate between DCIS and invasive cancers. If their analysis had included invasive cancers alone with a valid baseline of an annual increase of 1% and then compared the results with SEER data, they would have found fewer invasive cancers than predicted.

Screening Women at Increased Risk

Women with Prior History of Breast Cancer: These women should be treated according to the surveillance and follow-up recommendations outlined in [NCCN Guidelines for Breast Cancer](#).

Women Aged 35 Years or Older with a 5-Year Risk of Invasive Breast Carcinoma Greater Than or Equal to 1.7%: For women age 35 and older, a risk assessment tool is available to identify those who are at increased risk. The National Cancer Institute (NCI) and the National Surgical Adjuvant Breast and Bowel Project (NSABP) Biostatistics Center has developed a computerized interactive risk-assessment tool based on the modified Gail model²⁴⁻²⁸ that can be accessed at:

<http://www.cancer.gov/bcrisktool/Default.aspx> which provides risk projections on the basis of several risk factors for breast cancer. The modified Gail model assesses the risk of invasive breast cancer as a function of age, menarche, age at first live birth or nulliparity, number of first-degree relatives with breast cancer, number of previous benign breast biopsies, atypical hyperplasia in a previous breast biopsy, and race. The model calculates and prints 5-year and lifetime projected probabilities of developing invasive breast cancer and can be used to identify women who are at increased risk. The Gail model should not be used for women with a predisposing gene mutation, a strong family history of breast or ovarian cancer suggestive of a genetic predisposition, women with a prior history of thoracic radiation, or for those with LCIS.

The Gail model was updated using combined data from the Women's Contraceptive and Reproductive Experiences (CARE) study and the Surveillance Epidemiology and End Results (SEER) database, as well as causes of death from the National Center of Health Statistics, to provide a more accurate determination of risk for African-American women.²⁹ It has also been updated using the data from the Asian American Breast Cancer Study (AABCS) and the SEER database to provide a more accurate risk assessment for Asian and Pacific Islander women in the United States.³⁰

Increased risk of developing breast cancer is defined by the modified Gail model for women ≥ 35 years of age as a 5-year risk of 1.7% or greater. This is the average risk of a 60-year-old woman, which is the median age of diagnosis of breast cancer in the U.S. The 5-year predicted risk of breast cancer required to enter the NSABP Breast Cancer Prevention Trial of tamoxifen versus placebo, as well as the Study of Tamoxifen and Raloxifene (STAR) trial, was 1.7% or greater. As previously mentioned, the modified Gail model risk assessment tool

also provides an estimate of a woman's lifetime risk of breast cancer. However, this estimate is based on the Gail model risk criteria which differ from criteria used in risk assessment models predominantly based on family history (see below); lifetime breast cancer risk as determined by the Gail model is not used in these guidelines to determine whether a woman is eligible for screening breast MRI.

For a woman aged 35 years or older with a 5-year risk $\geq 1.7\%$, the NCCN Panel encourages breast awareness and recommends CBE every 6 to 12 months and annual mammography. In addition, according to the NCCN Panel, women in these groups should be asked to consider risk reduction strategies in accordance with the [NCCN Guidelines for Breast Cancer Risk Reduction](#).

Women with LCIS: A diagnosis of LCIS is associated with estimated risks of 10%-20% for the subsequent development of cancer in either breast over the next 15 years, although it is not in itself considered to be a site of origin for cancer.^{31,32}

For women with LCIS, the NCCN Panel encourages breast awareness and recommends CBE every 6 to 12 months and annual mammography beginning at diagnosis. In addition, according to the NCCN Panel, women in these groups should be asked to consider risk reduction strategies in accordance with the [NCCN Guidelines for Breast Cancer Risk Reduction](#).

Women with a Lifetime Risk of Breast Cancer >20% based on models largely dependent on family history: A lifetime risk of breast cancer of >20% as assessed by models based largely on family history is another risk threshold used in the guidelines to identify a woman as a potential candidate for risk reduction strategies, as well as to direct screening strategies. According to the ACS guidelines for breast screening, MRI

may be performed as an adjunct to mammography³³ in a high risk woman if her lifetime risk of breast cancer is approximately 20% or greater based on models that rely mainly on family history. A cancer genetic professional should be involved in determining the lifetime risk of the individual based on models dependent on family history. These include Claus,³⁴ Tyrer-Cuzick,³⁵ and other models³⁶⁻³⁸. BRCAPRO³⁹ and Breast and Ovarian Analysis of Disease Incidence and Carrier Estimation Algorithm (BOADICEA)⁴⁰ are more commonly used to estimate the risk based of *BRCA* mutations. Strong genetic association between breast and ovarian cancer has been demonstrated in some families by linkage analyses.

For a woman with a >20% lifetime risk of breast cancer based on models largely dependent on family history, the NCCN Panel encourages breast awareness and beginning at age 30, the NCCN Panel recommends CBE every 6 to 12 months and annual mammography. In addition, in accordance with the ACS guidelines,³³ the NCCN Panel recommends considering annual breast MRI for women who have a lifetime risk of breast cancer >20% based on models that rely mainly on family history. According to the NCCN Panel, women in this group should be asked to consider risk reduction strategies in accordance with the [NCCN Guidelines for Breast Cancer Risk Reduction](#).

Women Who Have Received Prior Thoracic Irradiation Between the Ages of 10 to 30 Years: Results from several studies have demonstrated that women who received thoracic irradiation in their second or third decade of life have a substantially increased risk of developing breast cancer by age 40 years.⁴¹⁻⁴⁶ For example, in the Late Effects Study Group trial, the overall risk of breast cancer associated with prior thoracic irradiation at a young age was found to be 56.7-fold (55.5-fold for female patients) greater than the risk of breast cancer in

the general population.^{42,45} In that study, the relative risk of female breast cancer according to follow-up interval was: 0 at 5-9 years; 71.3 at 10-14 years; 90.8 at 15-19 years; 50.9 at 20-24 years; 41.2 at 25-29 years; and 24.5 at > 29 years.⁴⁵ Results from a case-control study of women treated with thoracic radiation at a young age for Hodgkin lymphoma indicated that the estimated cumulative absolute risk of breast cancer at 55 years of age was 29.0% (95% CI, 20.2%-40.1%) for a woman treated at 25 years of age with at least 40 Gy of radiation and no alkylating agents.⁴⁷ Although there is a concern that the cumulative radiation exposure from mammography in a young woman may itself pose a risk for cancer, it is felt that the benefit of early detection of breast cancer in this high-risk group would outweigh the potential side effect. Findings from a survey of breast screening practices in this population of patients suggest that a sizable segment of this group is not undergoing regular mammographic screening.⁴⁸

For women aged 25 years and older who have received prior thoracic irradiation, the NCCN Panel recommends encouraging breast awareness, annual mammograms, annual MRI as an adjunct to mammograms⁴⁹ and CBE every 6 to 12 months be initiated 8 to 10 years after radiation exposure or 40, whichever comes first.⁵⁰

For women younger than 25 years who have received prior thoracic irradiation, the NCCN Panel recommends encouraging breast awareness, counseling on risk, and an annual CBE starting 8-10 years after the radiation therapy.

Women with a Pedigree Suggestive Of or With a Known Genetic Predisposition: Accurate family history information is needed to adequately assess a woman's breast cancer risk. Familial cancers share some but not all features of hereditary cancers. For example, although familial breast cancers occur in a given family more frequently

than expected on the basis of statistics, they generally do not exhibit inheritance patterns or onset age consistent with hereditary cancers. Familial breast cancers may be associated with chance clustering, genetic variations in lower-penetrance genes, a shared environment, small family size, and/or other factors.

The [NCCN Guidelines for Genetic/Familial High-Risk Assessment](#) include a recommendation for referral to a cancer genetics professional for further evaluation for an individual who has either a personal history or a close family history meeting any of the following criteria (see [NCCN Guidelines for Genetic/Familial High-Risk Assessment](#)).

In the statement on Genetic Testing for Cancer Susceptibility from the American Society of Clinical Oncology (ASCO) updated in 2003, genetic counseling/testing is recommended when there is: (i) a personal or family history suggesting genetic cancer susceptibility (ii) the test can be adequately interpreted and (iii) the results will aid in the diagnosis or influence the medical or surgical management of the patient or family members at hereditary risk of cancer.⁵¹ Additional genetic testing criteria are included in the [NCCN Guidelines for Genetic/Familial High-Risk Assessment](#). Genetic testing should be done only in the setting of pre-and post-test genetic counseling.

The manifestations of hereditary syndromes are often variable in individuals (e.g., age of onset, tumor site, and number of primary tumors). The risk of developing breast cancer in individuals with one of these hereditary syndromes depends upon numerous variables including the gender and age of the individual. Therefore there is variation in screening recommendations for different genetic syndromes. The [NCCN Guidelines for Genetic/Familial High-Risk Assessment](#) lists screening recommendations for common hereditary

syndromes that put the individuals at increased risk for breast and ovarian cancer.

Hereditary breast and ovarian cancer syndrome (HBOC): It has been estimated that over 90% of early onset cancers in families with both breast and ovarian cancers are caused by mutation(s) in the *BRCA1* or *BRCA2* genes.⁵² Hence, the degree of clinical suspicion for breast cancer in an individual with *BRCA* mutation or someone with a family history of both breast and ovarian cancer should be very high. The emphasis on initiating screening considerably earlier than standard recommendations is a reflection of the early age of onset seen in hereditary breast/ovarian cancer.^{38,53-55} The overall sensitivity of screening mammography was reported to be only 33% in a study of women with suspected or known *BRCA1/2* mutations who were more likely to be younger and to have dense breasts.⁵⁶ Other reasons for the low sensitivity of mammography in women with *BRCA1/2* mutations include an increased likelihood of developing tumors with more benign mammographic characteristics (e.g., less likely to appear as a spiculated mass).⁵⁷ The ACS recommends annual MRI as an adjunct to screening mammogram.³³

The risk from radiation exposure due to mammography in young women with an inherited cancer predisposition is unknown, and there is some concern about whether this genetic factor may increase sensitivity to irradiation. A recent study of *BRCA1/BRCA2* mutation carriers showed that lifetime mammogram exposure was not associated with an increased risk in breast cancer when the overall group was considered; however, a small increase in risk was seen when only those women with *BRCA1* mutations were evaluated.⁵⁸ Because the lifetime risk of breast cancer in *BRCA1* or *BRCA2* mutation carriers is estimated to be 3-6 fold greater (40% to 80% range)⁵⁹ than in the general population, the benefit of screening may justify the radiation exposure.

For a woman with a pedigree suggestive of a genetic predisposition or who is a carrier of a *BRCA1/2* mutation, the NCCN Panel recommends encouraging breast awareness and CBE every 6-12 months starting at age 25 years. The NCCN Panel also recommends screening women with annual mammograms and breast MRI as an adjunct to mammogram (MRI performed preferably on day 7-15 of menstrual cycle for premenopausal women) starting at age 25 years or on an individualized timetable based on the earliest age of cancer onset in family members. According to the NCCN Panel, women in this group should be offered risk reduction counseling and the opportunity to consider risk reduction strategies following multidisciplinary consultation in accordance with the [NCCN Guidelines for Breast Cancer Risk Reduction](#).

Male carriers of a *BRCA* gene mutation also have a greater risk for cancer susceptibility.⁶⁰ In one study of 26 high-risk families with at least one case of male breast cancer, 77% demonstrated a *BRCA2* mutation.⁵² However, among males with breast cancer who were not selected on the basis of family history, only 4%-14% tested positive for a germline *BRCA2* mutation.^{61,62} For males with a *BRCA2* mutation, the risk of breast cancer by age 80 years has been estimated at 6.9%.⁶³ A mutation in the *BRCA2* gene, accounts for about 1 in 10 breast cancers in men. *BRCA1* mutations can also cause breast cancer in men, but the risk is not as high as it is for mutations in the *BRCA2* gene. In contrast, for men without such a mutation, the lifetime risk of breast cancer has been estimated at about 1/10th of 1% (1 in 1,000).⁶⁴

The NCCN Panel recommendations for men positive for a *BRCA1/2* mutation include breast awareness and a CBE every 6-12 months starting at age 35. Baseline mammography should be considered at age 40 years, followed by annual mammography for those men with

gynecomastia or parenchymal/glandular breast density on baseline study.

Mammographic Screening

A screening mammogram typically involves 2 x-ray images of each breast (ie, one taken from the top [craniocaudal] of the breast and the other from the side [mediolateral oblique]). Randomized clinical trials have demonstrated that screening mammography lowers the rate of death from breast cancer,^{5,65} with a reported overall sensitivity of about 75%.⁶⁶ Nevertheless, the overall sensitivity of screening mammography was reported to be only 50% in a study of women with at least heterogeneous dense tissue,⁶⁷ and 33% in a study of women with suspected or known BRCA mutations who were more likely to be younger and to have dense breasts.⁵⁶

Technical aspects of mammography can affect the quality of screening results. Digital mammography differs from conventional film mammography in that the former generates an electronic image of the breast and allows for computer storage and manipulation. Four large scale trials have compared these two procedures although the designs and findings of these trials differ.⁶⁸⁻⁷³ In a study of 49,528 women who underwent both film and digital mammography, no difference was seen in the overall accuracy of the two procedures.^{68,69} However, digital mammography was significantly more accurate in younger women with dense breasts, and there was a nonsignificant trend toward improved accuracy of film mammography in women aged 65 years and older. In another trial of women aged 45 to 69 years randomly assigned to film or digital screening mammography, the latter procedure was shown to result in a higher rate of cancer detection.⁷⁰ Other outstanding issues related to these two procedures include possible differences in recall rates, and cost and availability issues.

Dense breast tissue as measured by mammography is increasingly recognized as an important risk factor for breast cancer.^{74,75} Although there are some studies supporting the use of ultrasound for breast cancer screening as an adjunct to mammography for high risk women with dense breast tissue,⁶⁷ the NCCN Panel however cautions that there is insufficient evidence to support routine supplemental screening in women with dense breasts and no other risk factors.

Mammographic Assessment Category Definitions:

Mammographic results are mandated to be reported using Final Assessment Categories [Breast Imaging Reporting and Data System (BI-RADS®)] categories developed by the American College of Radiology.[Mammography Quality Standards Act, 1997]⁷⁶ The purpose of the Final Assessment Category definitions is to create a uniform system of reporting mammography results with a recommendation associated with each category. The fourth edition of BI-RADS® is adopted in these guidelines. In this edition, substantive changes have been incorporated and category 6 has been added.⁷⁷

BI-RADS® assessment categories apply to an individual imaging method if only one type of imaging is done (eg, mammography), but if multiple imaging modalities are used (e.g. additional ultrasonography and MRI), the BI-RADS® categories represent the cumulative findings of the examinations that were performed. Therefore, the overall BI-RADS® assessment category can change depending on subsequent imaging findings (ie, the BI-RADS® assessment category given following a mammographic study may increase, decrease, or remain the same upon diagnostic ultrasonography or MRI). In the event that multiple abnormalities are identified on imaging, the overall final BI-RADS® assessment category is based on the most worrisome findings present. After the mammographic evaluation is completed, the results are classified according to one of the following BI-RADS® categories⁷⁶:

- **Category 1 - Negative:** This is a negative mammogram. The breasts are symmetric, and there are no masses, architectural distortion or suspicious calcification.
- **Category 2 - Benign Finding(s):** This is also a negative mammogram, but there may be an actual finding that is benign. The typical case scenarios include benign-appearing calcifications, such as a calcifying fibroadenoma, an oil cyst, or a lipoma. The interpreter may also choose to describe intramammary lymph nodes, vascular calcification, implants or architectural distortion clearly related to prior surgery while still concluding that there is no mammographic evidence of malignancy.
- **Category 3 - Probably Benign Finding(s) - Short-Interval Follow-up Suggested:** This is a mammogram that is usually benign. Close monitoring of the finding is recommended to ensure its stability. The risk of malignancy is estimated to be less than 2%.
- **Category 4 - Suspicious Abnormality –Biopsy Should Be Considered:** These lesions fall into the category of having a wide range of probability of being malignant but are not obviously malignant mammographically. The risk of malignancy is widely variable and is greater than that for category 3 but less than that for category 5.
- **Category 5 - Highly Suggestive of Malignancy-Appropriate Action Should Be Taken:** These lesions have a high probability ($\geq 95\%$) of being a cancer. They include spiculated mass or malignant-appearing pleomorphic calcifications, etc.
- **Category 6 - Known Biopsy - Proven Malignancy-Appropriate Action Should Be Taken:** This category is reserved for breast lesions identified on the imaging

study with biopsy proof of malignancy but prior to definitive therapies.

There is also another BI-RADS® category - Category 0 – which represents an incomplete assessment.

Category 0: Needs Additional Imaging Evaluation and/or Prior Mammograms For Comparison. This category is almost always used in the context of a screening situation, if a finding requiring additional evaluation has been identified. A recommendation for additional imaging evaluation may include, but is not limited to spot compression, magnification, special mammographic views and ultrasound. Under certain circumstances, this category may be used after a full mammographic workup. Whenever possible, if the study is not negative and does not contain a typical benign finding, the current examination should be compared to previous studies. The radiologist should use judgment on how vigorously to attempt obtaining previous studies. The practice guideline for the performance of screening and diagnostic mammography from the American College of Radiology can be accessed at:

http://www.acr.org/SecondaryMainMenuCategories/quality_safety/guidelines/breast/Screening_Diagnostic.aspx.

NCCN Recommendations after Mammographic Evaluation

For patients with mammograms classified as BI-RADS® categories 1 and 2, in which the mammogram is completely normal or the finding is benign mammographically, the NCCN Panel recommends routine screening, based on age and risk of breast cancer. When screening mammography reveals an abnormal finding, the radiologist should attempt to obtain any prior mammograms. This is most important for lesions that are of low suspicion mammographically. If, after a comparison of films, there is still a questionable area that is not clearly benign, then a diagnostic mammogram (see section on “Diagnostic

Mammography” on MS-11), with or without ultrasonography (see section on “Breast Ultrasonography” on MS-12) should be performed.

For NCCN recommendations and follow-up of patients with mammograms categorized as BI-RADS® 0 and 3 or higher, see section on “Diagnostic Evaluation for Positive Findings” on MS-11.

Breast Magnetic Resonance Imaging Screening

The sensitivity of breast MRI at detecting breast cancer is higher than the sensitivity of mammography, although the specificity of the former procedure is lower, resulting in a higher rate of false-positive findings.⁷⁸ In addition, microcalcifications are not detectable with MRI,^{79,80} and the issue of whether breast MRI screening impacts survival has not been addressed in randomized clinical trials. Therefore, careful patient selection for additional screening with MRI is needed. Although current evidence does not support the use of breast MRI to screen women at average risk of breast cancer, benefits of screening MRI for women with prior thoracic radiation, and those with a genetic predisposition for breast cancer have been demonstrated in several studies,^{49,56,81-87} and the ACS has published guidelines recommending use of breast MRI as an adjunct to screening mammography in certain populations of women at high risk of breast cancer.³³ Nevertheless, a high false-positive rate for screening MRI was identified in several these studies. For example, in one study of high-risk women, many of whom were young and had very dense breast tissue, screening MRI led to 3 times as many benign biopsies as mammography.⁵⁴

A single retrospective study of asymptomatic women with atypical hyperplasia or LCIS enrolled in a high-risk screening program has evaluated use of MRI in this population.⁸⁸ Approximately half of the women underwent screening with mammography and MRI whereas the other half was screened with mammography alone. For those undergoing

both types of screening, breast cancer was detected by MRI in 4% of patients with LCIS who had negative mammogram results. MRI screening did not impact the rate of cancer detection in women with atypical hyperplasia. Women who underwent screening with MRI were more likely to be younger and premenopausal, and to have a stronger family history of breast cancer than those who were evaluated by mammography alone. However, only one woman with cancer detected by MRI following a negative mammography finding had reported a family history of breast cancer, and no difference was seen in the percentages of patients who ultimately developed cancer in the 2 groups.

The NCCN Panel recommends an annual MRI as an adjunct to screening mammogram and CBE for the following groups with increased risk of breast cancer: 1) Women with a pedigree suggestive of or known genetic predisposition for breast cancer, starting at age 25 for HBOC, or individualized based on earliest age of onset in the family and 2) Women who received with thoracic radiation therapy between ages 10 to 30 years (MS-6). MRI may be considered as an adjunct to screening mammogram for women with a >20% lifetime risk of breast cancer as defined by models largely based on family history as described in the ACS guidelines.⁴⁰

Criteria for the performance/interpretation of high quality breast MRI include: a dedicated breast coil, radiologists experienced in breast MRI; and the ability to perform MRI-guided needle sampling and/or wire localization of MRI-detected findings. Breast MRI Guidelines from the European Society of Breast Imaging include detailed descriptions of the technical aspects of the use of breast MRI.⁷⁸ The American College of Radiology has also published guidelines for the performance of contrast-enhanced MRI of the breast.⁸⁹

Diagnostic Evaluation for Positive Findings

Additional evaluations in selected patients with positive findings can include diagnostic mammography, ultrasonography, diagnostic breast MRI, and tissue sampling.

Diagnostic Mammography

Screening mammography which consists of 2 standard X-ray images of each breast differs from diagnostic mammography in that the latter is used to evaluate a patient with a positive clinical finding—such as a breast lump or an abnormal screening mammogram. A diagnostic mammogram includes additional views, such as spot compression views or magnifications views, to investigate the finding in question.

NCCN Recommendations for Mammogram BI-RADS® **Assessment Categories 0, 3, 4, 5 and 6**

For BI-RADS® category 0 (need additional imaging evaluation), the diagnostic work-up includes comparison to prior films and/or diagnostic mammogram with or without ultrasound scan.

For BI-RADS® category 3 (probably benign), diagnostic mammograms at 6 months, then every 6 to 12 months for 2 to 3 years are appropriate. At the first 6-month follow-up, a unilateral mammogram of the index breast is performed. The 12-month study would be bilateral in women aged 40 years and older so that the contralateral breast is imaged at the appropriate yearly interval. Depending on the level of concern, the patient is then followed, either annually with bilateral mammograms or every 6 months for the breast in question, for a total of 2 to 3 years.

If the lesion remains stable or resolves mammographically, the patient resumes routine screening intervals for mammography. If, in any of the

interval mammograms, the lesion increases in size or changes its benign characteristics, a biopsy is then performed. The exception to this approach of short-term follow-up is when a return visit is uncertain or the patient is highly anxious or has a strong family history of breast cancer. In those cases, initial biopsy with histologic sampling may be a reasonable option.

For BI-RADS® categories 4 and 5, tissue diagnosis using core needle biopsy (preferred) or needle localization excisional biopsy with specimen radiograph is necessary. When a needle biopsy (aspiration or core needle biopsy) is performed, concordance between the pathology report and the imaging finding must be obtained.^{77,90} For example, a negative needle biopsy associated with a spiculated category 5 mass is discordant and clearly would not be an acceptable diagnosis. When the pathology and the imaging are discordant, the breast imaging should be repeated and/or additional tissue sampled or excised; surgical excision is recommended when pathology/image remain discordant. Women with a benign result exhibiting pathology/image concordance should be followed with mammography every 6-12 months for 1-2 years before returning to routine screening.

For BI-RADS® category 6 (proven malignancy), the patient should be managed according to the [NCCN Guidelines for Breast Cancer](#).

Breast Ultrasonography

Mammography and ultrasound are complementary imaging methods for diagnosing breast cancer. However, breast ultrasonography does not detect most microcalcifications.^{56,67,91-93}

Initial diagnostic imaging with breast ultrasonography is recommended as the preferred option for women aged < 30 years presenting with a palpable mass or asymmetric thickening/nodularity. Breast

ultrasonography is recommended for women ≥ 30 years of age with a palpable mass and a diagnostic mammogram assessed as BI-RADS® 1-3, and as an adjunct to diagnostic mammography for women in this age group with a finding of asymmetric thickening/nodularity. In addition, breast ultrasonography should be considered as an adjunct to mammography for those of all ages with skin changes consistent with serious breast disease or with spontaneous nipple discharge in the absence of a palpable mass, and as a possible option for women with a BI-RADS® category 0 screening mammographic assessment. Consideration of follow-up ultrasound testing is also recommended when initial ultrasound findings of a solid mass are classified as a probably benign finding, or when biopsy results are found to be benign and image concordant. Ultrasound-guided biopsy is included in the guidelines for women with a complex cyst or a persistent mass following cyst aspiration.

Ultrasonographic Assessment Category Definitions:

After the ultrasonographic evaluation is completed, the results are classified according to one of the following BI-RADS® categories.⁹⁴

- **Category 0 – Needs Additional Imaging Evaluation.** This represents an incomplete assessment. A finding for which additional evaluation is needed. If ultrasound is the initial study, mammography might be indicated, or if mammography and ultrasound findings are nonspecific, MRI might be appropriate.
- **Category 1 - Negative:** This is a negative ultrasound. No abnormalities are detected.
- **Category 2 - Benign Finding(s):** This is also a negative ultrasound, but there may be an actual finding that is benign. Included in this category are simple cysts (see section below on “Breast cysts”) and breast implants.

- **Category 3 - Probably Benign Finding(s) - Short-Interval Follow-up Suggested:** This is a ultrasound that is usually benign. Close monitoring of the finding is recommended to ensure its stability. The risk of malignancy is estimated to be less than 2%. Fibroadenomas and nonpalpable complicated cysts and clustered microcysts might be placed in this category for short-interval follow-up (see section below on “Breast cysts”).
- **Category 4 - Suspicious Abnormality –Biopsy Should Be Considered:** These lesions fall into the category of having a wide range of probability of being malignant but are not obviously malignant ultrasonographically. The risk of malignancy is widely variable and is greater than that for category 3 but less than that for category 5. A complex cyst would be included in this group (see section below on “Breast cysts”).
- **Category 5 - Highly Suggestive of Malignancy-Appropriate Action Should Be Taken:** These lesions have a high probability ($\geq 95\%$) of being a cancer.
- **Category 6 - Known Biopsy - Proven Malignancy-Appropriate Action Should Be Taken:** This category is for breast lesions identified on the imaging study with biopsy proof of malignancy but prior to definitive therapies.

Breast Cysts

Breast cysts are either classified as simple or non-simple cysts, with the latter class being subdivided into complicated cysts and complex cysts (see [Table 1](#) for definitions).

Simple cyst

A cyst meeting all criteria of a simple cyst is considered to be benign,^{67,95} if the clinical findings and ultrasonographic results are concordant. Therapeutic fluid aspiration can be considered if clinical

symptoms persist, and these patients can be followed with routine screening. Cytologic examination is recommended if bloody fluid is obtained.

Non-simple Cysts

A complicated non-simple cyst is associated with a low risk of malignancy (<2%).^{67,96-98} Options for managing complicated cysts are either aspiration or short-term follow-up with physical examination and ultrasonography with or without mammography every 6-12 months for 2-3 years to assess stability. There may be variability on the follow-up interval based on the level of suspicion. The option of aspiration may be more strongly considered in a patient likely to be lost to follow-up. Complicated cysts which increase in size should be biopsied. As with simple cysts, cytologic analysis of fluid aspirated from a complicated cyst is required only if bloody fluid is obtained. In the event of a persistent mass, a biopsy is needed.

For cysts which resolve following aspiration but are characterized by bloody fluid, the NCCN Panel recommends placement of a tissue marker followed by cytologic evaluation of fluid. Follow-up of a positive finding includes percutaneous vacuum-assisted biopsy or excision. If findings are negative, physical examination with or without ultrasound/mammogram every 6-12 months for 1-2 years is recommended to assess stability. Repeat imaging (ultrasound with or without mammogram) is recommended for a recurrent mass whereas routine screening is the recommended strategy when follow-up examinations are negative.

Complex cysts have a relatively high risk of malignancy (eg, 14% and 23% in 2 studies).^{67,97-100} Hence, these cysts should be evaluated by tissue biopsy.

Diagnostic Breast MRI

MRI can also play a role in the diagnostic setting. For patients with skin changes consistent with serious breast disease, consideration of breast MRI is included in the guidelines for those with benign biopsy of skin or nipple following BI-RADS® category 1-3 assessment. Since a benign skin punch biopsy in a patient with a clinical suspicion of inflammatory breast cancer (IBC) does not rule out malignancy, further evaluation is recommended. There is evidence that certain MRI features may facilitate diagnosis of IBC.¹⁰¹

Breast Tissue Biopsy

Breast biopsy is recommended if diagnostic mammogram and/or ultrasound findings are suspicious or highly suggestive of malignancy.

Fine Needle Aspiration (FNA) Biopsy

An FNA biopsy involves use of a smaller-bore needle to obtain cytologic samples from a breast mass. Advantages of FNA biopsy include its minimally invasive methodology and low cost,^{102,103} whereas the need for pathologists with specific expertise in the interpretation of test results and the necessity of performing a follow-up tissue biopsy when atypia or malignancy is identified are disadvantages of the procedure. FNA of nonpalpable lesions can be performed under imaging guidance (eg, ultrasound), although there is evidence to indicate that both core-needle biopsy and excisional biopsy are more accurate than FNA in the evaluation of nonpalpable breast lesions.^{104,105}

Core Needle Biopsy

A core needle biopsy, also called percutaneous core breast biopsy, is an automated procedure that typically involves obtaining multiple cores of solid tissue using standard techniques.^{106,107} It can be performed under imaging guidance (eg, stereotactic [mammographic] or ultrasound). Advantages of breast core needle biopsy include increased

accuracy over FNA when the procedure is performed in situations where no mass is palpable and an ability to obtain tissue samples of sufficient size so as to eliminate the need for a follow-up biopsy to confirm malignancy.¹⁰⁸ In some situations, the core needle biopsy is performed under vacuum assistance which can facilitate collection of adequate tissue from a breast lesion without the need for multiple needle insertions.^{109,110} Clip placement is done at the time of core needle biopsy so that the radiologist can identify the location of the lesion in the event that it is entirely removed or disappears during neoadjuvant treatment of a breast cancer.¹¹¹ With a few exceptions, core needle biopsy is preferred in the NCCN Guidelines over surgical excision when tissue biopsy is required. According to the NCCN panel, surgical excision is appropriate if unable to perform core needle biopsy

Excisional Biopsy

An excisional biopsy involves removal of the entire breast mass or suspicious area of the breast by a surgeon in an operating room setting. Needle or wire localization is done by the radiologist immediately prior to an excisional biopsy of a nonpalpable mammographic or sonographic finding to direct surgical excision. The wire localization may bracket a lesion that had a clip placed in it at the time of the core needle biopsy.¹¹¹

Excisional biopsy is included in the NCCN Guidelines as an option when tissue biopsy is required. Although excisional biopsy is a more invasive method than core needle biopsy and requires needle localization when lesions are not palpable, there are situations where larger tissue samples may be needed. In most cases, excisional biopsy is recommended following diagnosis by core biopsy of an indeterminate lesion, atypical hyperplasia, LCIS, or a benign and image discordant lesion. Other histologies that may require additional tissue include mucin-producing lesions, potential phyllodes tumor, papillary lesions, radial scars or other histologies of concern to the pathologist.^{100,103,108,112}

Support for this recommendation includes results of studies demonstrating an underestimation of cancer when atypical hyperplasia and LCIS are diagnosed by CNB.¹¹³⁻¹¹⁸ However, there are situations (eg, select cases of LCIS, ALH, papillomas, fibroepithelial lesions, radial scars) where close observation may be substituted for excisional biopsy in select patients.^{103,112,119-125}

Physical Examination

Symptomatic or positive findings on physical examination include: palpable mass in the breast, nipple discharge without a palpable mass, asymmetric thickening or nodularity, and skin changes

NCCN Recommendations for Positive Findings on Physical Exam

Palpable Mass in the Breast

A palpable mass is a discrete lesion that can be readily identified during a physical exam. The guidelines separate the evaluation of women with the palpable mass into two age groups: women aged 30 years or older and women under 30 years of age.

Women with palpable mass aged 30 years or older:

The main difference in the guidelines for evaluating a palpable mass in women age 30 or older compared with younger women is the increased degree of suspicion of breast cancer. The initial evaluation begins with a bilateral diagnostic mammogram. Observation without further evaluation is not an option in these women. There are some clinical circumstances such as mass with low clinical suspicion or suspected simple cyst, in which ultrasound would be preferred and may suffice for women 30-39 years of age.¹²⁶ After the mammographic assessment, the abnormality is placed in one of the six BI-RADS® categories.

For women with BI-RADS® categories 4 and 5, assessment of the geographic correlation between clinical and imaging findings is indicated. If the imaging findings correlate with the palpable findings, the NCCN Panel recommends tissue evaluation through core needle biopsy. The NCCN Panel notes that fine needle aspiration (FNA) and core needle biopsy are both valuable. However, FNA requires cytologic expertise. When a core needle biopsy is utilized, concordance between the pathology report and imaging finding must be obtained. If there is a lack of geographic correlation between clinical and imaging findings, further evaluation is as recommended for BI-RADS® categories 1, 2, or 3.

For BI-RADS® categories 1, 2, and 3, the next step is to obtain an ultrasound and the findings are discussed below under “Ultrasound findings”.

Ultrasound findings:

If the solid lesion found on the ultrasound is suspected to be probably benign (ie, BI-RADS® 3), the options are: observation, or core needle biopsy. Observation may be elected only if there is low clinical suspicion, in which case a physical examination with or without ultrasound or mammogram is recommended every 6 months for 2-3 years to assess stability. If the option of core needle biopsy is elected, and the result is benign and is concordant with the imaging results, the NCCN Panel recommends a physical examination every 6 to 12 months, with or without ultrasound or mammogram, for 1 to 2 years to ensure that the lesion is stable. Routine breast screening is recommended if the lesion is stable. If the solid lesion increases in size, the NCCN Panel recommends surgical excision. If the diagnosis by core biopsy is an indeterminate lesion, atypical hyperplasia, LCIS, or a benign and image discordant lesion, the NCCN Panel recommends surgical excision. Mucin-producing lesions, potential phyllodes tumor,

papillary lesions, radial scars or other histologies of concern to the pathologist may also require excisional biopsy. Select patients (ie, some patients with atypical hyperplasia, LCIS, fibroepithelial lesions, radial scars etc) may be suitable for monitoring in lieu of surgical excision.

If the ultrasound evaluation reveals the mass to be consistent with an asymptomatic simple cyst (ie, BI-RADS® 2), the NCCN Panel recommends routine screening. However, it is important that there is concordance between the CBE and the ultrasound results before recommending routine screening. Therapeutic aspiration of such a simple cyst can be performed if persistent clinical symptoms are present.

If the cyst on the ultrasound is classified as a complicated non-simple cyst, options include aspiration or short-term follow-up (BI-RADS® 3). For short term follow-up, the NCCN Panel recommends physical examination and ultrasound with or without mammography every 6-12 months for 2-3 years to assess stability. A tissue biopsy should be performed for a complicated cyst which increases in size during follow-up.

Alternatively, aspiration may be performed. If blood-free fluid is obtained on aspiration, the mass resolves, and cytology results are negative, the NCCN Panel recommends that the patient should return to routine screening. If the mass first resolves after aspiration and then recurs, then repeat assessment with ultrasound or surgical excision if warranted. If the mass persists after aspiration, the NCCN Panel recommends ultrasound with image-guided biopsy. Surgical excision is appropriate if unable to perform core needle biopsy.

For cysts that resolve following aspiration but are characterized by bloody fluid, the NCCN Panel recommends placement of a tissue

marker followed by cytologic evaluation of fluid. Follow-up of a positive finding includes percutaneous vacuum-assisted biopsy or excision. If findings are negative, physical examination with or without ultrasound/mammogram every 6-12 months for 1-2 years is recommended to assess stability. Repeat imaging is recommended for a recurrent mass whereas routine screening is the recommended strategy when follow-up examinations are negative. The NCCN Panel recommends a tissue biopsy for cysts classified as complex (BI-RADS® 4).

If the ultrasound with image-guided biopsy findings are benign and image concordant (BI-RADS® 1), physical exam with or without ultrasound or mammogram every 6-12 months for 1-2 years is recommended. If the mass increases in size, surgical excision should be repeated, with a routine breast screening recommended if the mass remains stable. If the ultrasound and image guided biopsy findings are interpreted as benign and image discordant or indeterminate or atypical hyperplasia or LCIS or other (ie, mucin-producing lesions, potential phyllodes tumor, papillary lesions, radial scar or other histologies of concern to the pathologist), surgical excision is recommended, although select patients (ie, some patients with atypical hyperplasia, LCIS, fibroepithelial lesions, radial scars, etc.) may be suitable for monitoring in lieu of surgical excision (see section on “Excisional Biopsy” on MS-14). Multifocal/extensive LCIS involving 4 terminal ductal lobular units on a core biopsy may be associated with increased risk of invasive cancer on surgical excision.

If the mass has been surgically excised and proven to be benign, the patient undergoes routine screening. If the mass is classified as atypical hyperplasia or LCIS, routine breast screening along with risk reduction therapy according to the [NCCN Guidelines for Breast Cancer Risk Reduction](#) is recommended.

If no ultrasonographic abnormality is detected (BI-RADS® 1), tissue biopsy (core needle biopsy or excision) or observation at 3-6 months intervals for 1-2 years should be considered to assess stability. If the lesion increases in size, tissue sampling should be repeated, whereas routine breast screening is recommended if the lesion remains stable.

Malignant findings either on ultrasound with image guided biopsy or surgical excision should be treated according to the [NCCN Guidelines for Breast Cancer](#).

Women with palpable mass under 30 years of age:

The preferred option for initial evaluation of a palpable mass is to proceed directly to ultrasound with or without mammogram.¹²⁶ From this point, the decision tree for women under 30 years of age is almost identical to the pathway for older women. The main difference is consideration of a diagnostic mammogram in only some situations for the younger women. Because the degree of suspicion in women who are under the age of 30 is low, observation of the mass for one or two menstrual cycles is also an option in cases with low clinical suspicion. If observation is elected and the mass resolves after one or two menstrual cycles, the patient may return to routine screening. If the mass persists, ultrasound should be performed. Needle sampling prior to imaging is not recommended.

If no ultrasonographic abnormality is found (BI-RADS® 1), a mammogram is recommended in cases where there is high clinical suspicion or those at higher risk due to known genetic mutation or family history. Based on the mammogram results, from this point, the management is identical to the pathway for older women. Whereas if the clinical suspicion is low, observation every 3-6 months for 1-2 years is recommended. If the mass increases in size during the observation period, mammogram may be considered followed by

tissue biopsy. If the mass remains stable, routine breast screening is recommended.

Nipple Discharge without a Palpable Mass

Nipple discharge is common, and, in many cases, unrelated to breast pathology.¹²⁷⁻¹³³ For example, non-spontaneous discharge from multiple breast ducts in a non-lactating woman can occur during pregnancy, following breast stimulation, in women with certain thyroid conditions, and in those taking certain medications, such as estrogen, oral contraceptives, opiates, and particular antihypertensive agents.¹²⁷ Suspicion of underlying pathology (eg, papilloma, ductal ectasia) is raised when nipple discharge is persistent and reproducible on examination, spontaneous, unilateral, from a single duct with fluid characterized as clear and colorless, serous, sanguineous, or serosanguineous.¹³⁴

In patients with a nipple discharge but no palpable mass, an evaluation of the characteristics of the nipple discharge is the first step. The appropriate follow-up of a non-spontaneous, multiple-duct discharge in women under age 40 is observation, coupled with education of the patient to stop compression of the breast and to report the development of any spontaneous discharge. In women aged 40 years or older, screening mammography and a further workup based upon the BI-RADS® category along with education similar to that for younger women is recommended. Evaluation of this type of nipple discharge is based on the overall BI-RADS® category of the diagnostic mammogram with or without adjunctive ultrasound.

Mammary ductoscopy is useful in evaluating patients who have nipple discharge, for accurate visualization, analysis, and excision of intraductal abnormalities.¹³⁵⁻¹³⁷ Magnetic resonance imaging (MRI) may

play an adjunctive role, aiding in the differentiation of benign ductal abnormalities from malignant ones. Preliminary studies have shown that breast MRI aids in the diagnosis of suspected ductal disease and is an alternative to ductoscopy when the latter cannot be used.^{138,139}

According to the NCCN Panel, for an overall BI-RADS® assessment category 1, 2, or 3, either a ductogram or MRI (optional) is recommended to guide the duct excision. Ductal excision is indicated for diagnosis of an abnormal nipple discharge, even if the ductogram is negative.¹⁴⁰ However, the ductogram is useful to exclude multiple lesions and to localize the lesions prior to surgery.

For an overall BI-RADS® assessment category 4 or 5, the NCCN Panel recommends a tissue biopsy. If the findings are benign or indeterminate, a ductogram is optional, but surgical duct excision would still be necessary. If findings are indicative of malignancy, the patient should be treated according to the [NCCN Guidelines for Breast Cancer](#).

Asymmetric Thickening or Nodularity

Thickening, nodularity, or asymmetry is distinct from a palpable mass in that the finding is ill defined and often vague on physical breast examination. Factors to consider include whether the thickening is a new or previous finding, and whether or not it appears to be representative of normal asymmetry. If the patient is under the age of 30 years and has no high risk factors, ultrasound evaluation is appropriate followed by consideration of diagnostic mammography. Diagnostic mammograms for this age group are fairly low in yield because of the density of the breast and low risk of breast cancer. In a woman aged 30 years or older, a bilateral diagnostic mammogram, and an ultrasound evaluation should be obtained.

If a clinically suspicious change is noted or the overall imaging findings are classified as BI-RADS® assessment category 4-5 a tissue biopsy is recommended.

If the overall imaging findings are classified as BI-RADS® category 1-3 *and* the clinical assessment is benign, the patient should be reexamined in 3 to 6 months to assess stability. For BI-RADS® category 3, the physical exam is followed by ultrasound and/or mammogram every 6-12 months for 2-3 years. If the findings on physical and/or imaging is stable, routine screening can be resumed. If the finding shows clinical progression, it should be investigated as previously described for palpable mass.

Skin Changes

Any type of unusual skin changes around the breast may represent serious disease and needs evaluation. Inflammatory breast cancer (IBC) should be considered when dermal edema (peau d'orange) and breast erythema are present, and nipple excoriation, scaling, and eczema should increase clinical suspicion of Paget's disease. IBC is a rare, aggressive form of breast cancer estimated to account for 1%-6% of breast cancer cases in the U.S. IBC is a clinical diagnosis that requires erythema and dermal edema of a third or more of the skin of the breast with a palpable border to the erythema.^{141,142} Paget's disease of the breast is a rare manifestation of breast cancer characterized by neoplastic cells in the epidermis of the nipple areolar complex. It most commonly presents with eczema of the areola, bleeding, ulceration, and itching of the nipple. The diagnosis is often delayed because of the rare nature of the condition and confusion with other dermatologic conditions.^{143,144}

The management of patients with IBC or Paget's disease is outlined in [NCCN Guidelines for Breast Cancer](#).

The initial evaluation of a patient with breast skin changes begins with a bilateral diagnostic mammogram with or without ultrasound imaging. If the imaging results are abnormal, the evaluation proceeds on the basis of the imaging findings. If the breast imaging results are normal, further workup is still needed.

Punch biopsy of skin or nipple biopsy should be performed following imaging findings consistent with an overall BI-RADS® assessment category 1-3. Antibiotics may or may not be given, depending on the clinical scenario, but should not delay diagnostic evaluation. If biopsy results are benign, clinical and pathological correlation should be reassessed. In addition, a breast MRI, a repeat biopsy, and consultation with a breast specialist should be considered. If the skin biopsy is malignant, the patient should be treated according to the [NCCN Guidelines for Breast Cancer](#).

A tissue biopsy should be performed if imaging findings are consistent of an overall BI-RADS® assessment category 4-5. According to the NCCN Panel, core needle biopsy is the preferred option with or without punch biopsy although surgical excision is also an option. A benign biopsy result should be followed by a punch biopsy of skin if not previously performed or nipple biopsy, with reassessment as described above for BI-RADS® category 1-3. A biopsy showing a malignant finding should be managed according to the [NCCN Guidelines for Breast Cancer](#).

Summary

The intent of these guidelines is to give health care providers a practical, consistent framework for screening and evaluating a spectrum of breast lesions. Clinical judgment should always be an important component of the optimal management of the patient.

If the physical breast examination, radiologic imaging, and pathologic findings are not concordant, the clinician should carefully reconsider the assessment of the patient's problem. Incorporating the patient into the health care team's decision-making empowers the patient to determine the level of breast cancer risk that is personally acceptable in the screening/follow-up settings.



Table 1: Breast Cysts - Types and Definitions

Simple cyst	Anechoic (cystic), well circumscribed, round or oval with well-defined imperceptible wall and posterior enhancement.
Non-simple cyst	Has one or more characteristics not found in a simple cyst.
<ul style="list-style-type: none"> • complicated 	Has most but not all elements of a simple cyst. Complicated cysts do not contain solid elements, intracystic masses, thick walls, or thick septa. This type of cyst may contain low-level echoes or intracystic debris, and can be described as a round, circumscribed mass containing low level echoes without vascular flow, fulfilling most but not all criteria of a simple cyst.
<ul style="list-style-type: none"> • complex 	Has some discrete solid component which may include thick walls, thick septa, and/or intracystic mass. Complex cysts have both anechoic (cystic) and echogenic (solid) components.
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Discussion
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