

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

Breast Cancer Screening and Diagnosis

Version 2.2013

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NCCN Guidelines Version 2.2013 Panel Members

Breast Cancer Screening and Diagnosis

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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](#).

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Summary of the changes in the 2.2013 version of the Breast Cancer Screening and Diagnosis Guidelines from the 1.2013 version include:

[MS-1](#) The discussion section was updated to reflect the changes in the algorithm.

[BSCR-5](#) Footnote “l” has been modified to include an age group, as follows; “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.” (Also for BSCR-14).

Updates in Version 1.2013 of the NCCN Guidelines for Breast Cancer Screening from Version 1.2012 include:

[BSCR-1](#)

- For “clinical breast exam every 1-3 years,” changed the age on the upper branch to “Age ≥ 25 but < 40 y.” Changed “normal risk” to “average risk.”

[BSCR-2](#)

- Under Increased Risk, last branch: added “between the ages of 10 and 30 y” to “Prior thoracic RT.”
- Under Screening Follow-up: last branch, first bullet, first sub-bullet modified to read, “Begin 8-10 y after RT or age 40, whichever comes first.”

[BSCR-6](#)

- Changed follow-up intervals to 2-3 years for consistency with BI-RADS® and included a new footnote “v” for intervals regarding clinical suspicion that reads, “There may be variability on the follow-up interval based on the level of suspicion.” (Also for BSCR-12, BSCR-14).
- Modified footnote “t” to include, “Surgical excision is appropriate if unable to perform core needle biopsy.” (Also for BSCR-8, BSCR-15, BSCR-17).

[BSCR-8](#)

- Footnote “y” is new to the page, “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.” (Also for BSCR-17).

[BSCR-11](#)

- Added “ \pm mammogram” to the first branch after “Palpable mass age < 30 .”

[BSCR-12](#)

- First branch modified to, “Consider mammogram as clinically indicated.”
- Added a new branch for BI-RADS® category 3, coming off “Consider mammogram as clinically indicated.”

[BSCR-13](#)

- The top branch off “Persistent and reproducible ...” now reads: “Age < 30 y Ultrasound \pm mammogram”
- The bottom branch off “Persistent and reproducible...” now reads: “Age ≥ 30 y Mammogram \pm ultrasound.”

[BSCR-14](#)

- Added “Simple cyst” as the first branch off BI-RADS category 1-2 Negative, or benign findings.

[BSCR-A \(1 of 2\) and \(2 of 2\)](#)

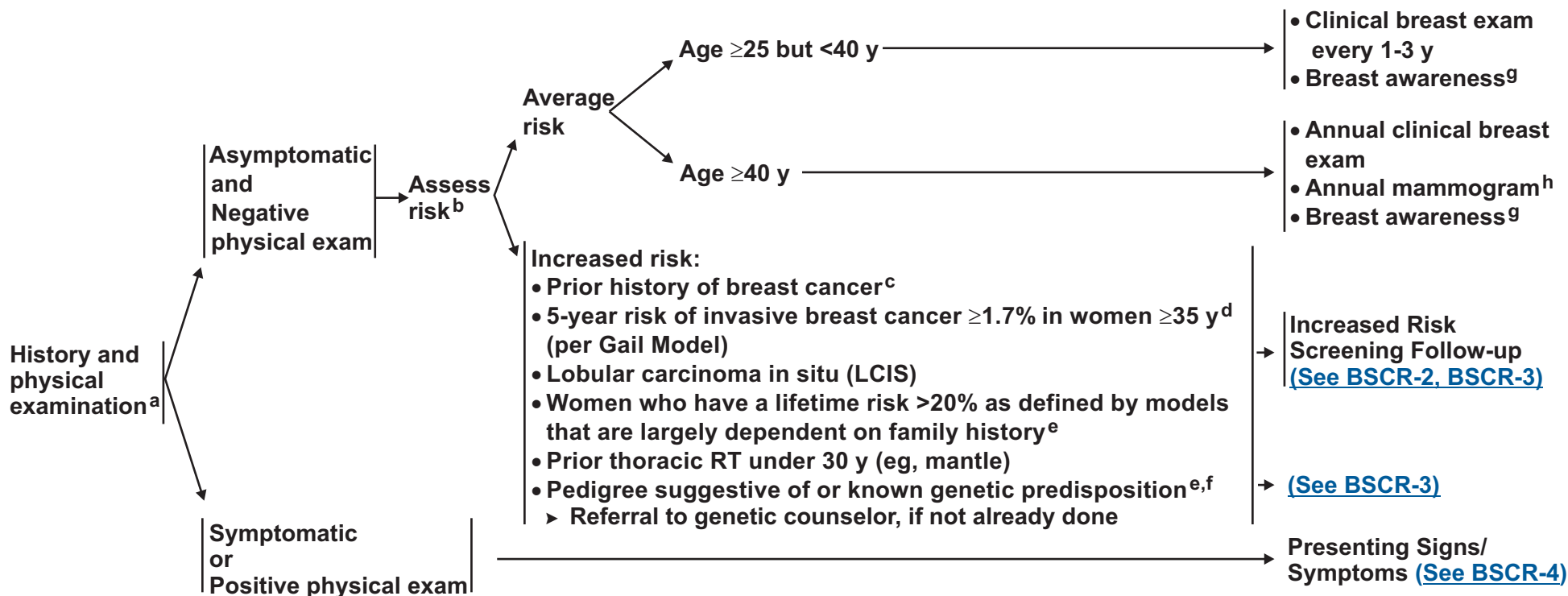
- Added a reference to the 5th bullet under Insufficient Evidence to Recommend for or Against MRI Screening: Brennan S, Liberman L, Dershaw DD, et al. Breast MRI Screening of Women with a Personal History of Breast Cancer. AJR 2010;195:510-516.

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SCREENING OR SYMPTOM CATEGORY

SCREENING FOLLOW-UP^a



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

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

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

^d See [Risk Factors Used in the Modified Gail Model \(BSCR-B\)](#).

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

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

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

^h See [Mammographic Evaluation \(BSCR-16\)](#).

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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 mammogram^h + clinical breast exam every 6-12 mo
 - Breast awareness^g
 - Consider risk reduction strategies ([See NCCN Guidelines for Breast Cancer Risk Reduction](#))

OR

LCIS (begin screening at diagnosis)

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

-
- Annual mammogram^h + clinical breast exam every 6-12 mo
 - ▶ beginning at age 30 y
 - Breast awareness^g
 - Consider risk reduction strategies ([See NCCN Guidelines for Breast Cancer Risk Reduction](#))
 - Consider annual breast MRI
 - ▶ beginning at age 30 y

Prior thoracic RT between the ages of 10 and 30 y

Age <25 y

Age ≥25 y

-
- Annual clinical breast exam
 - ▶ beginning 8 to 10 y after RT
 - Breast awareness^g
-
- Annual mammogram^h + clinical breast exam every 6-12 mo
 - ▶ Begin 8-10 y after RT or age 40, whichever comes first
 - Recommend annual breast MRI as an adjunct to mammogram and clinical breast exam
 - Breast awareness^g

^d[See Risk Factors Used in the Modified Gail Model \(BSCR-B\).](#)

^eRisk models that are largely dependent on family history (eg, Claus, BRCA1, BRCA2, 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. 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.

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SCREENING OR SYMPTOM CATEGORY

SCREENING FOLLOW-UP FOR HBOC

Increased Risk:

Pedigree suggestive of or known genetic predisposition^{e,f}
 • Hereditary breast and ovarian cancer (HBOC)^f



WOMEN

- Breast awareness^g
- Clinical breast exam, 6-12 mo,ⁱ starting at age 25 y
- Annual mammogram^h and breast MRI^j screening starting at age 25 y, or individualized based on earliest age of onset in family^k
- Consider risk reduction strategies ([See NCCN Guidelines for Breast Cancer Risk Reduction](#))

MEN

- Breast awareness
- Clinical breast exam, every 6-12 mo, starting at age 35 y
- Consider baseline mammogram at age 40 y; annual mammogram^h if gynecomastia or parenchymal/glandular breast density on baseline study

^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.](#)

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

^hSee Mammographic Evaluation ([BSCR-16](#)).

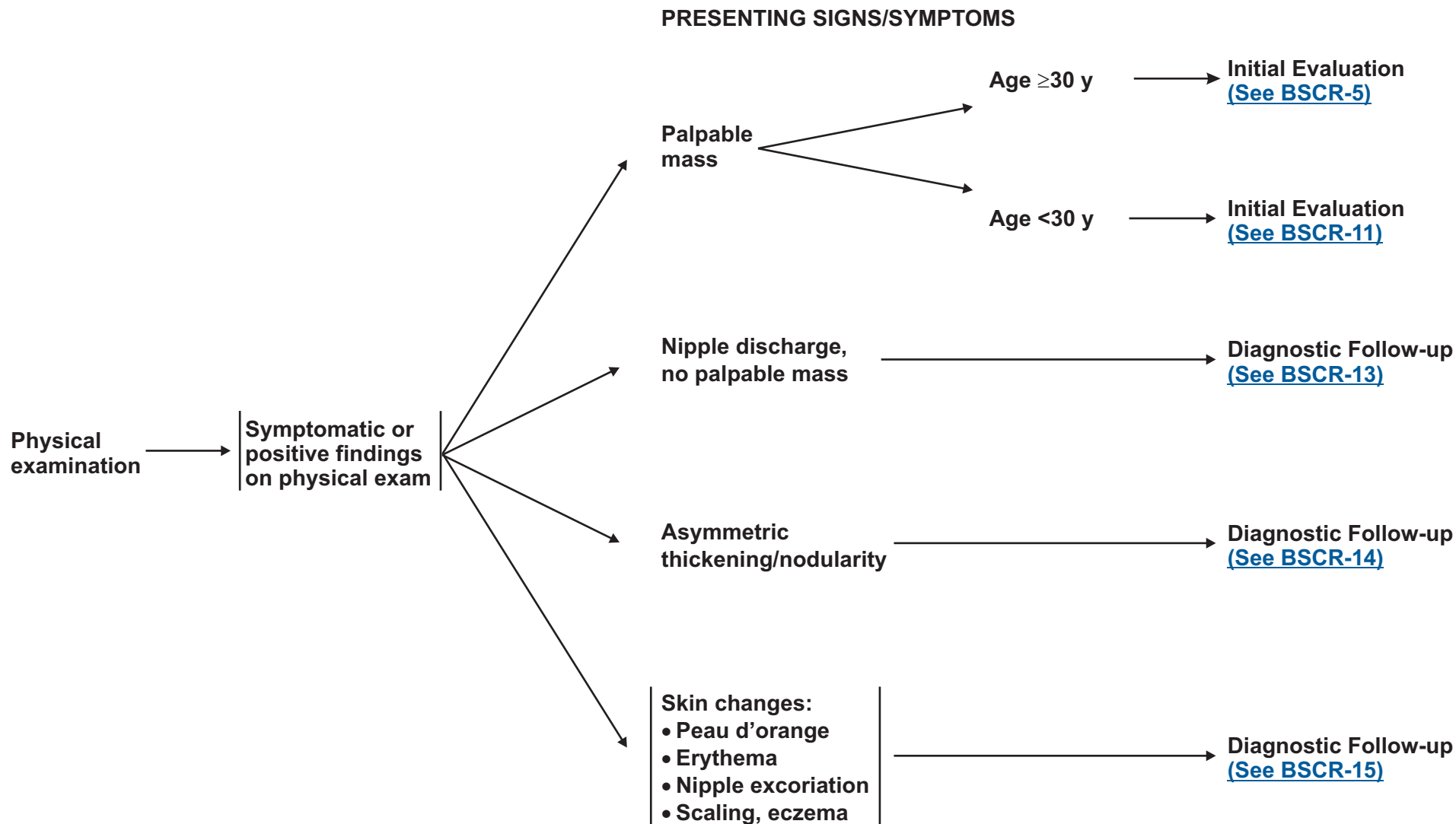
ⁱRandomized trials comparing clinical breast exam versus no screening have not been performed. Rationale for recommending clinical breast exam every 6-12 mo is the concern for interval breast cancers.

^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.

^kThe appropriateness of imaging scheduling is still under study.

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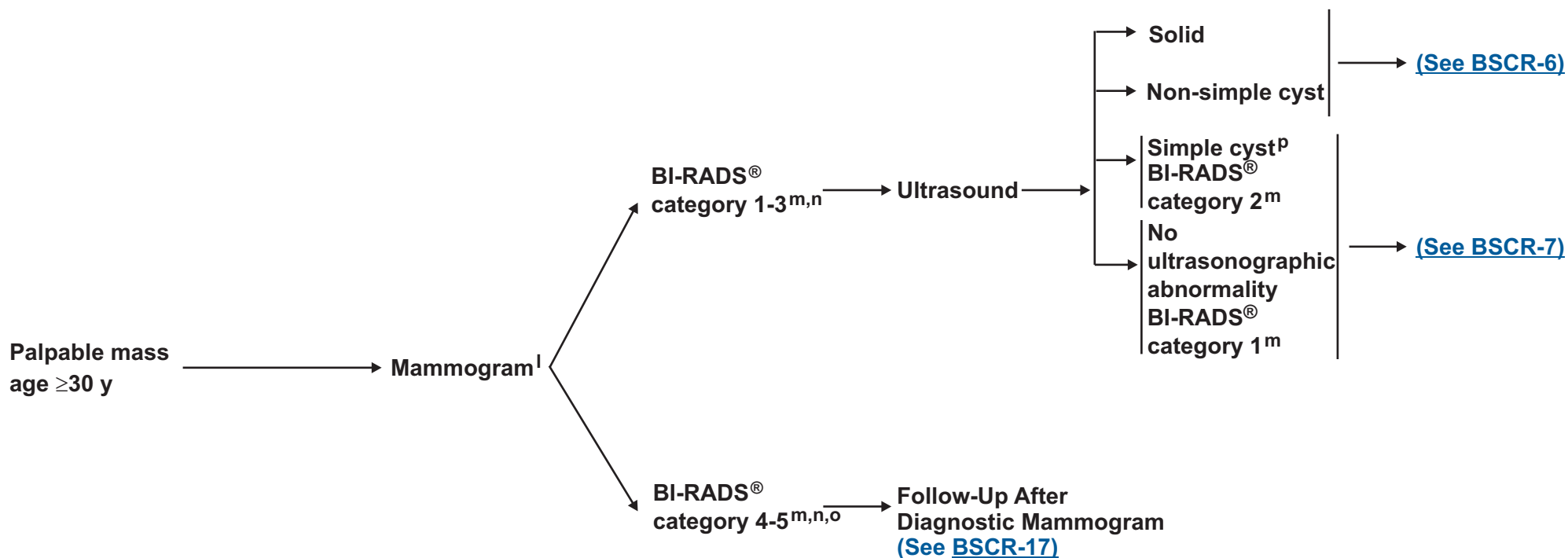
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**PRESENTING
SIGNS/SYMPTOMS**

INITIAL EVALUATION

ULTRASOUND FINDINGS



^IThere 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.](#)

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

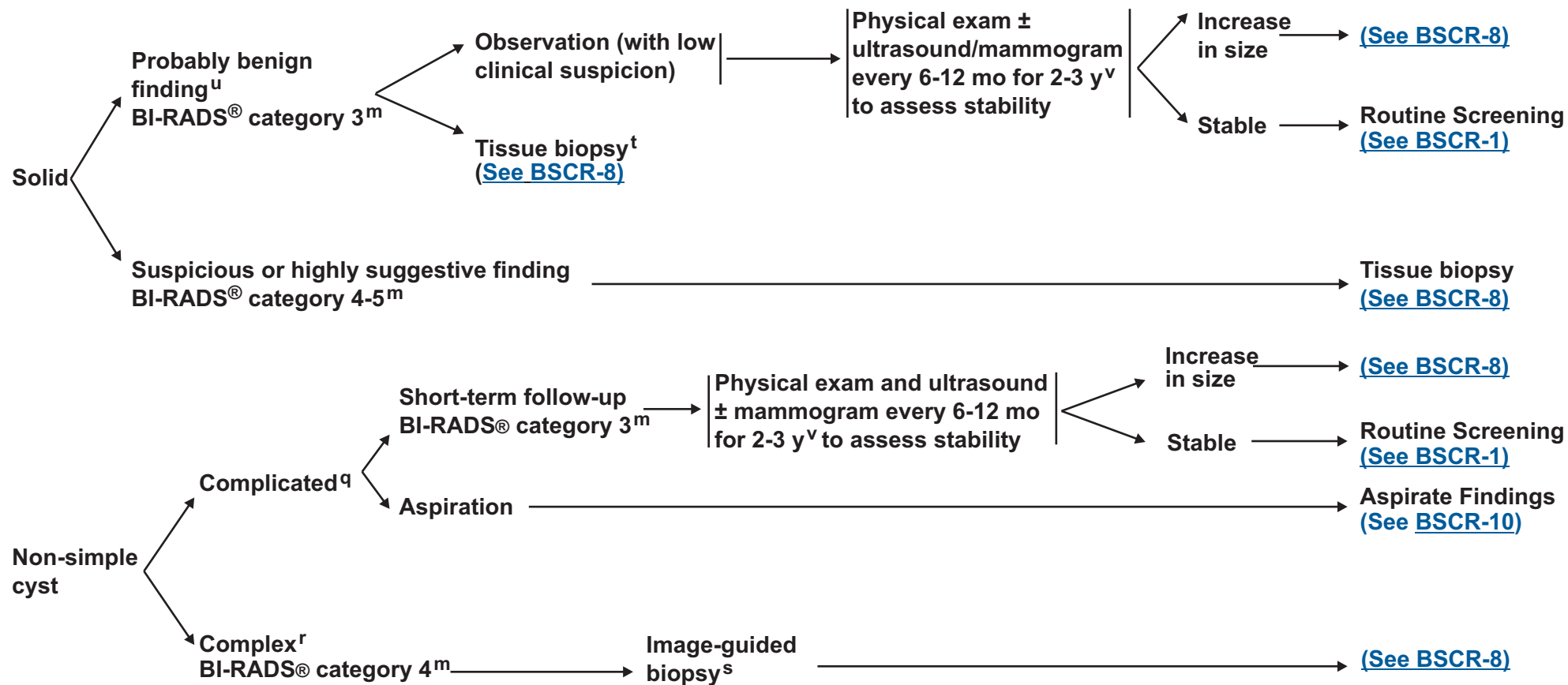
ⁿMammography results are mandated to be reported using Final Assessment categories (Quality Mammography Standards: Final Rule. Federal Register. 1997;62:55988).

^oAssess 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.

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

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ULTRASOUND FINDINGS/PALPABLE MASS



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

^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.

^sSurgical excision if image-guided/core needle biopsy is not possible.

^tFNA 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.

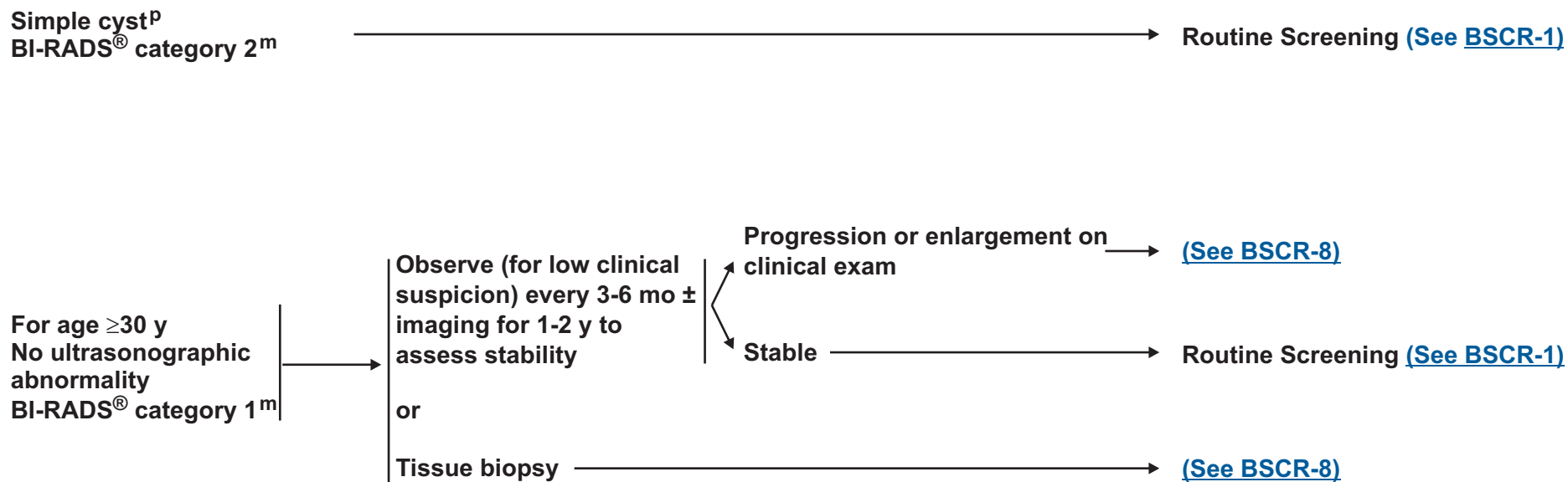
^uStavros A, Thickman D, Rapp C, et al. Solid breast nodules: Use of sonography to distinguish between benign and malignant lesions. *Radiology* 1995;196:123-124.

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

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ULTRASOUND FINDINGS/PALPABLE MASS



^mSee Assessment Category Definitions (BSCR-C).

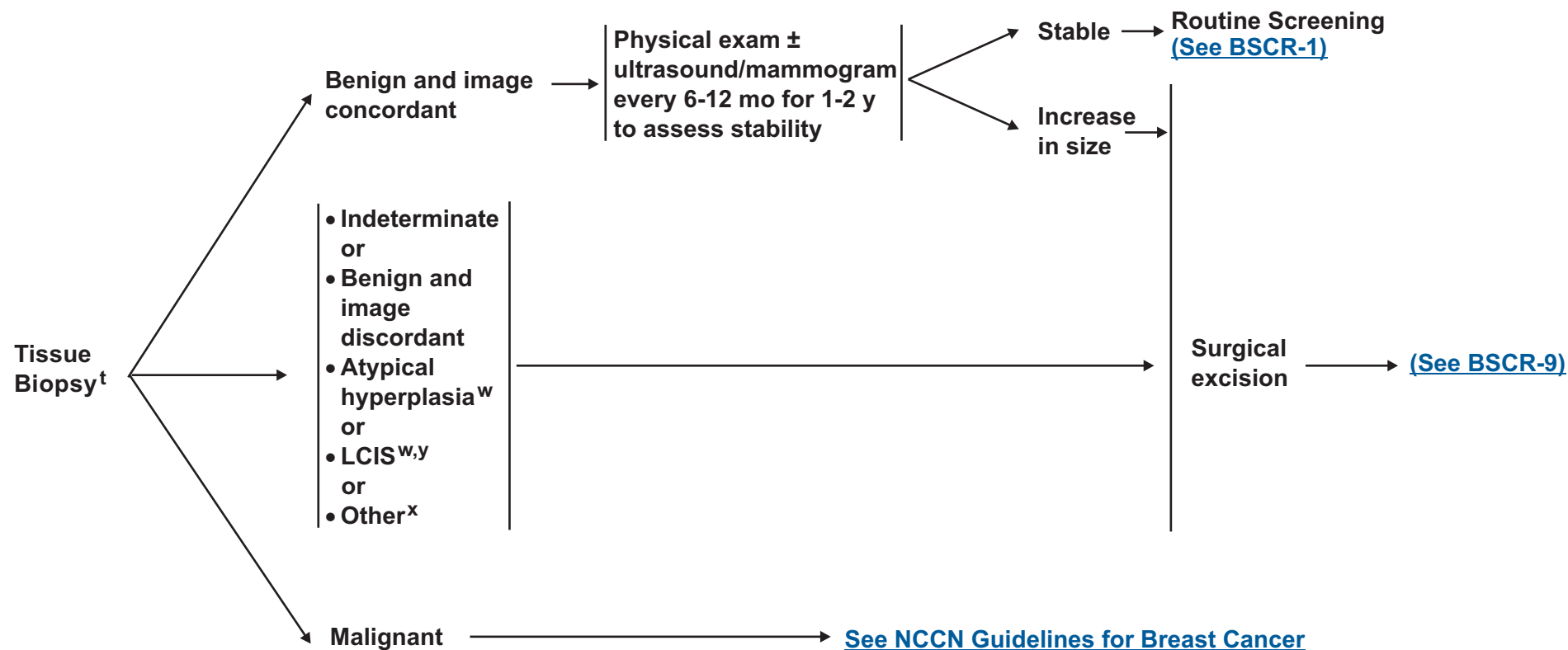
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PALPABLE MASS

FOLLOW-UP EVALUATION



^tFNA 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.

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

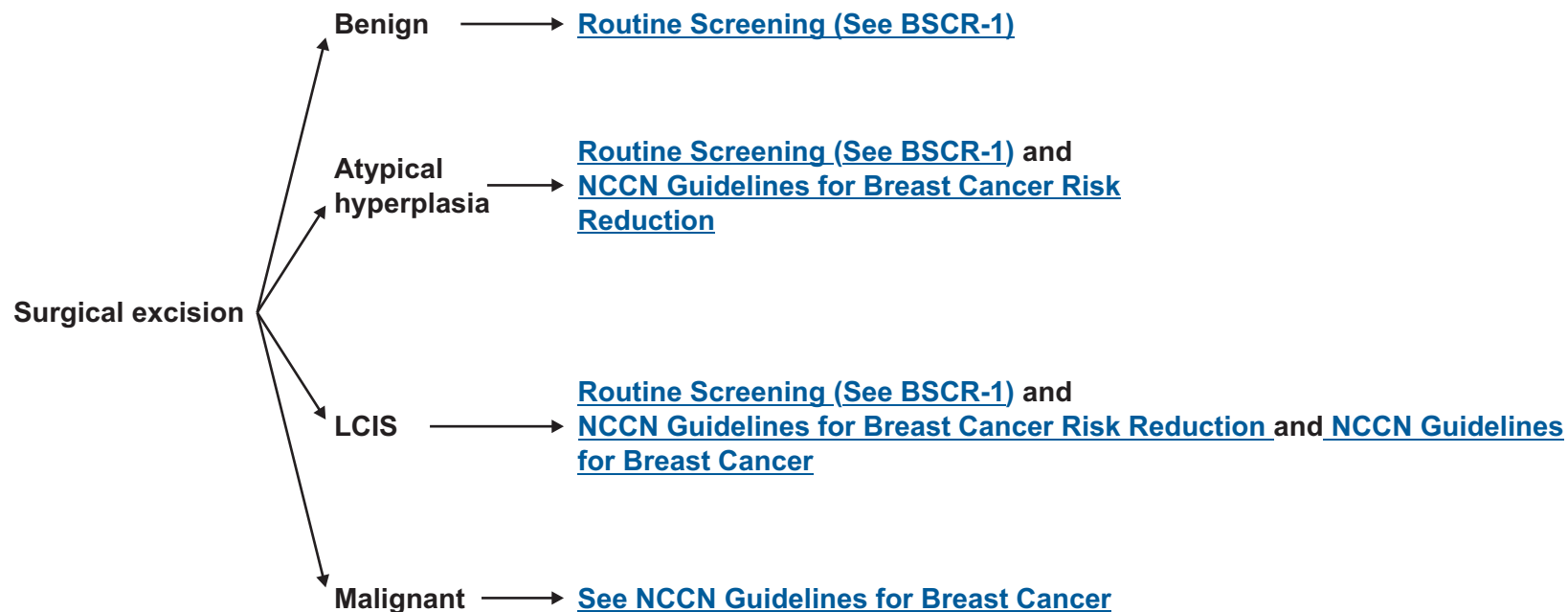
^xOther histologies that may require additional tissue: mucin-producing lesions, potential phyllodes tumor, papillary lesions, radial scar, or histologies of concern to pathologist.

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

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FOLLOW-UP EVALUATION

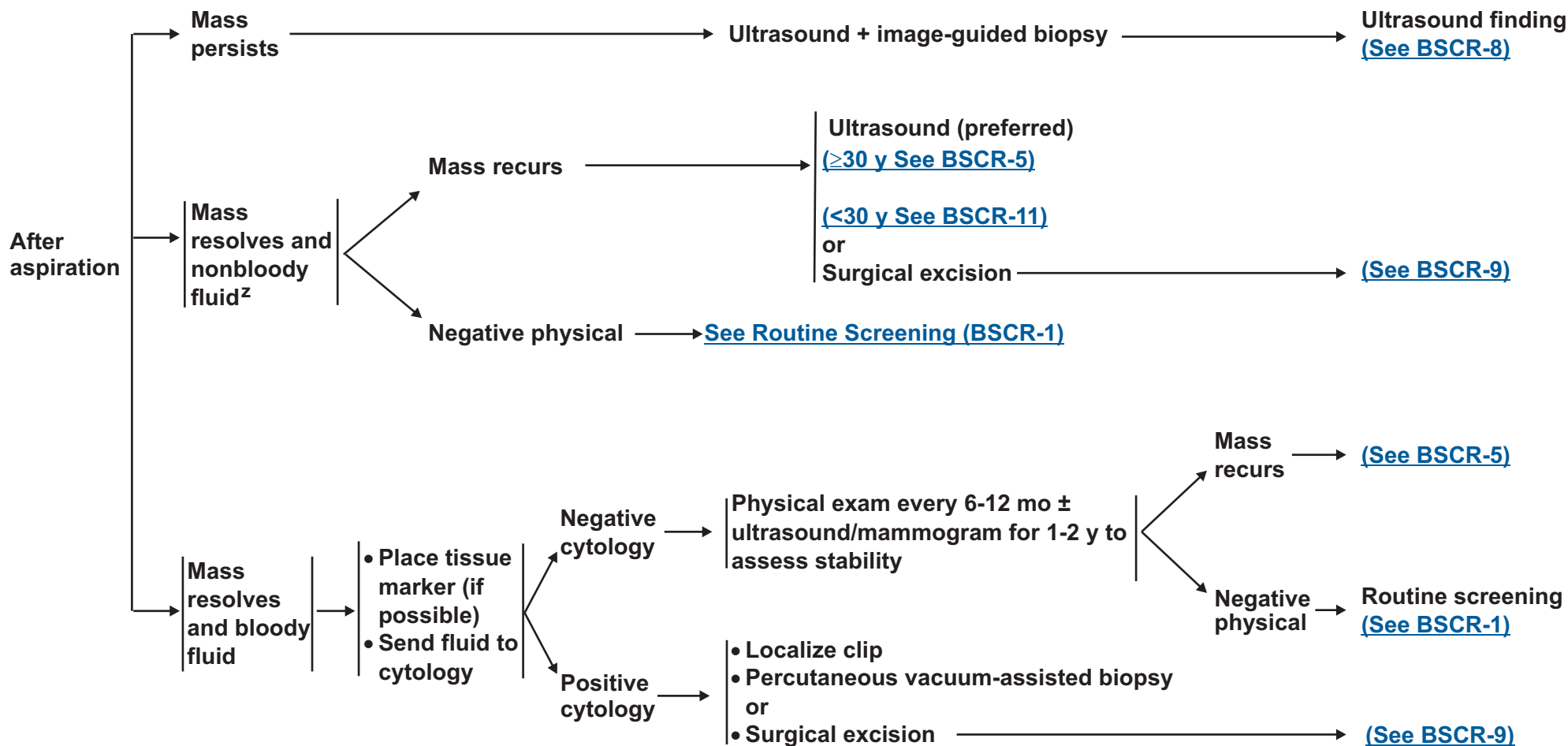


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ASPIRATE FINDINGS/PALPABLE MASS

FOLLOW-UP EVALUATION



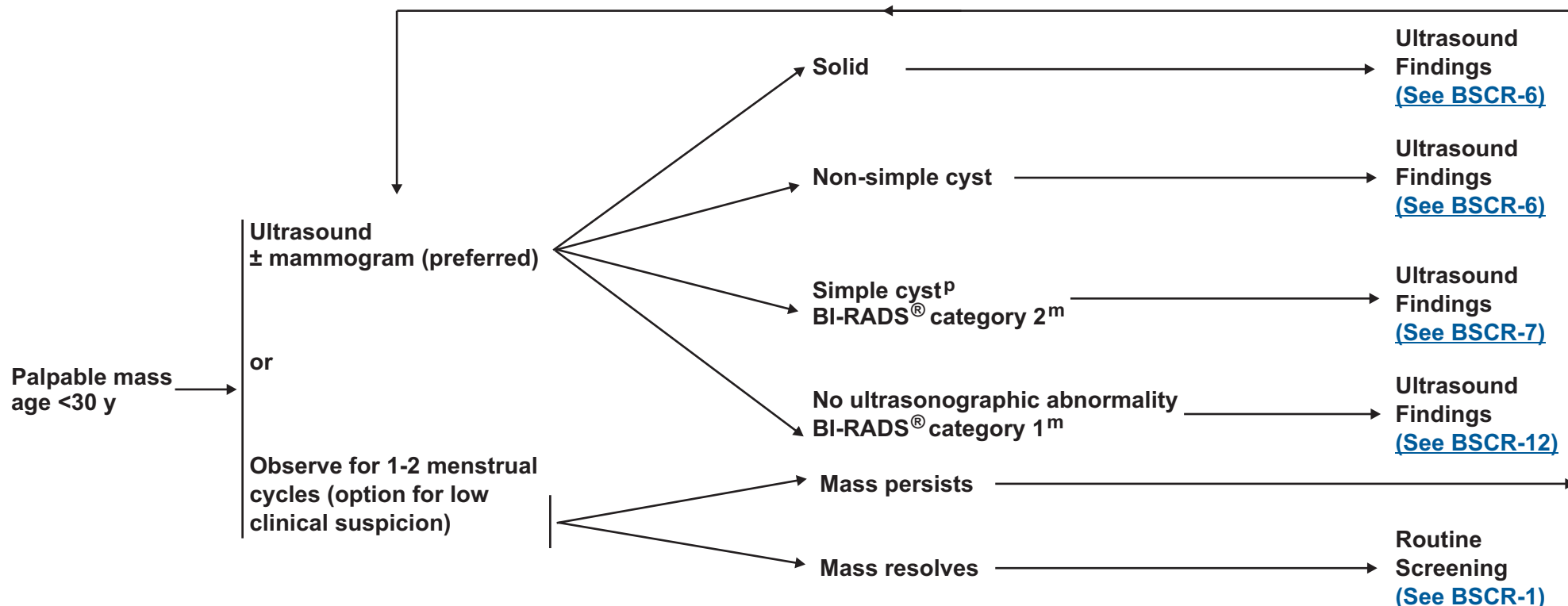
²Routine cytology not recommended.

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PRESENTING SIGNS/SYMPTOMS

INITIAL EVALUATION



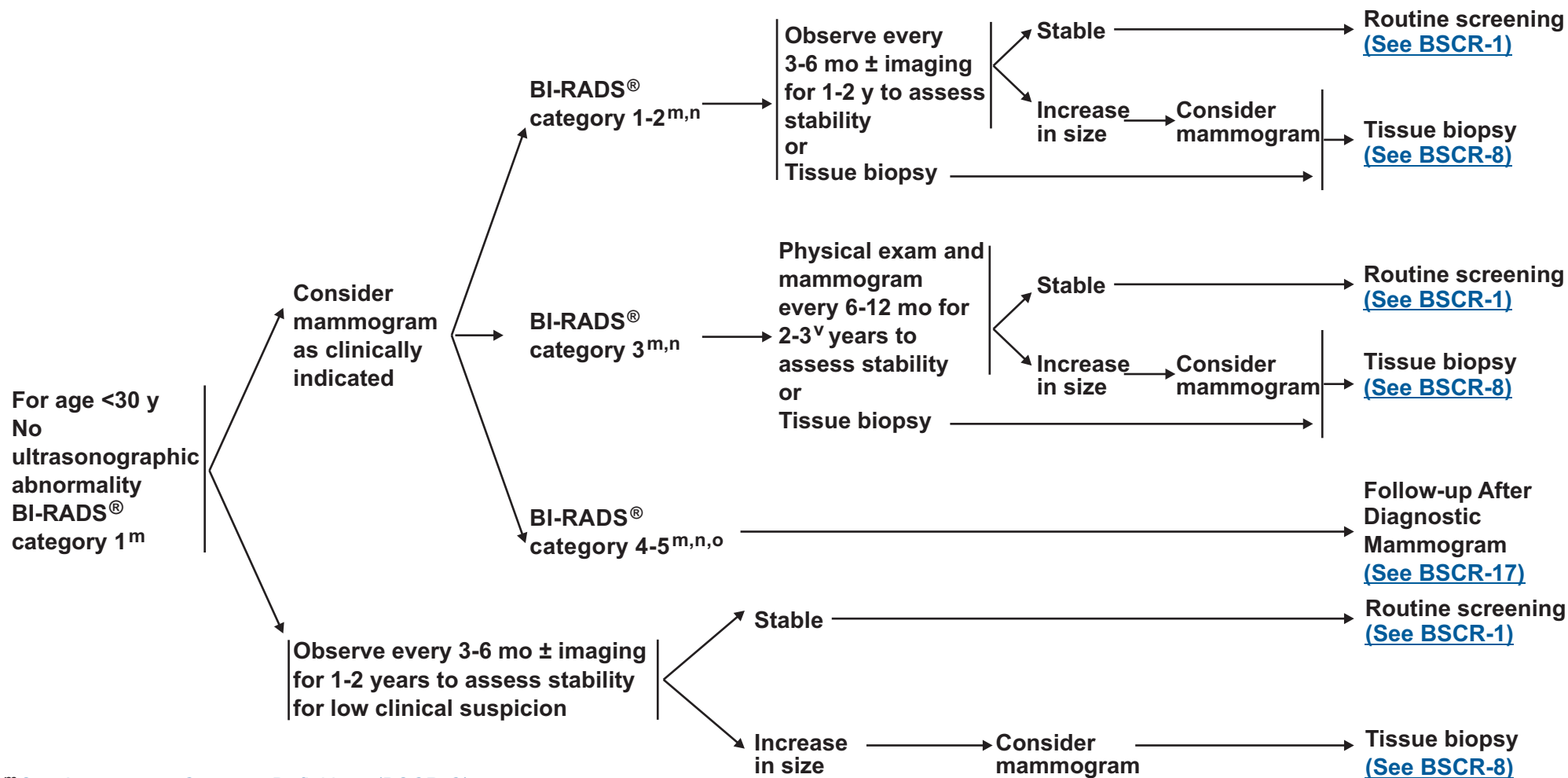
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ULTRASOUND FINDINGS/PALPABLE MASS

FOLLOW-UP EVALUATION



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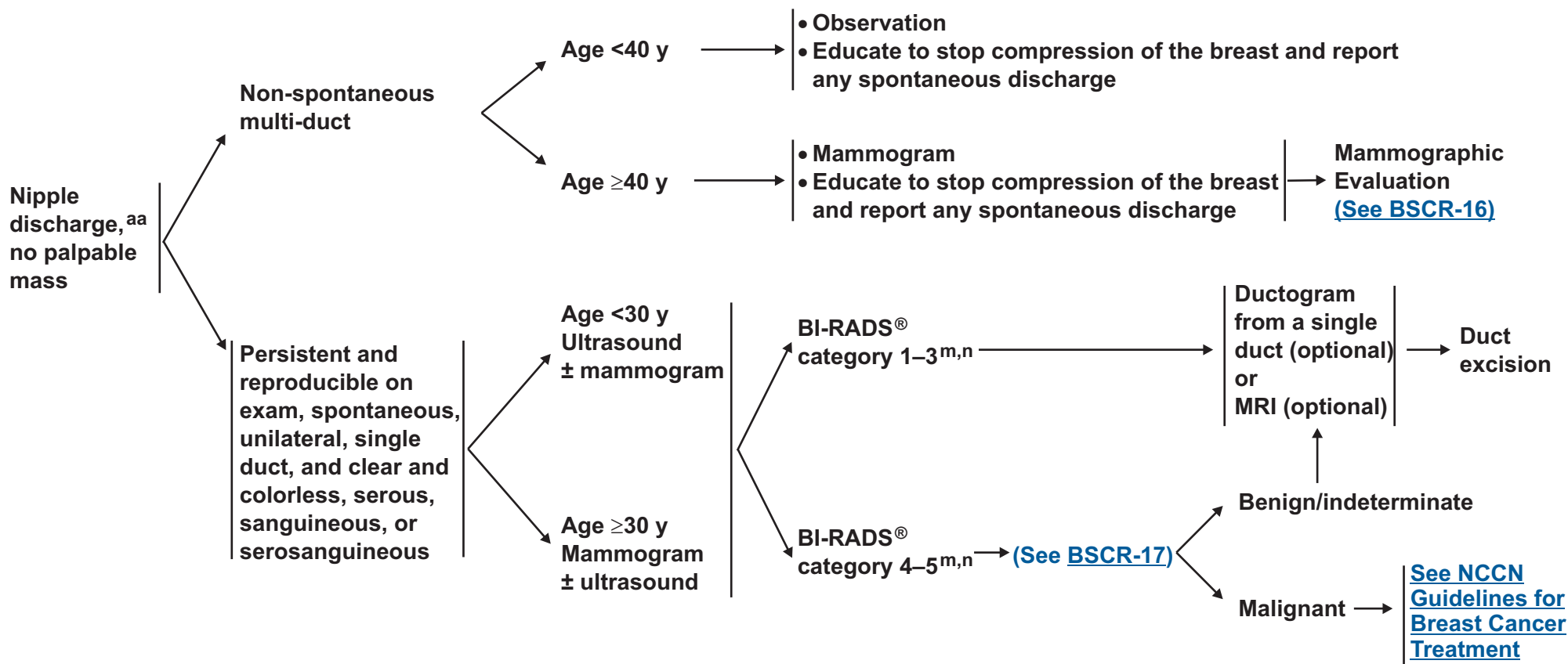
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PRESENTING SIGNS/ SYMPTOMS

DIAGNOSTIC FOLLOW-UP



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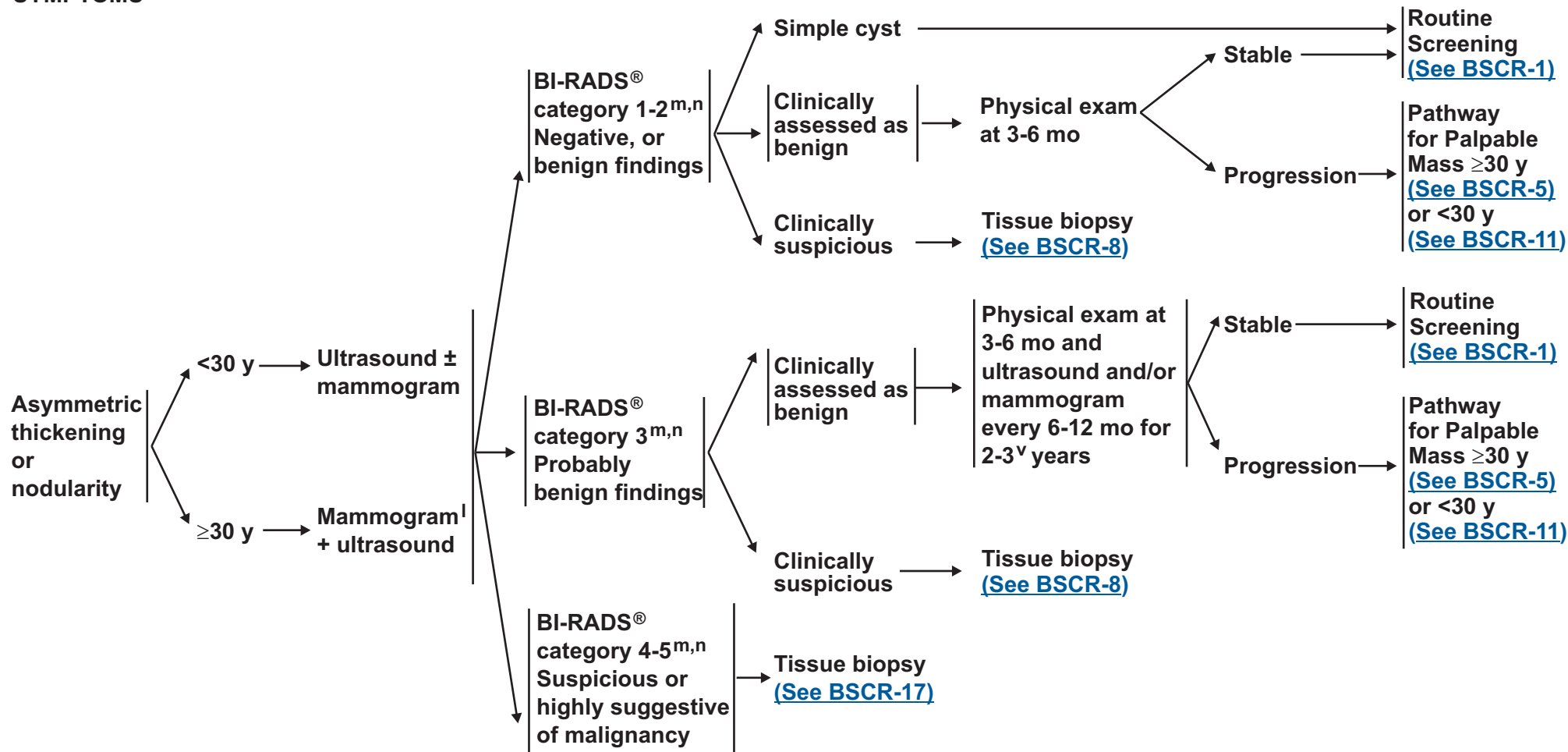
^{aa}A list of drugs that can cause nipple discharge (not all-inclusive): Psychoactive drugs, antihypertensive medications, opiates, oral contraceptives, and estrogen.

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**PRESENTING SIGNS/
SYMPTOMS**

DIAGNOSTIC FOLLOW-UP



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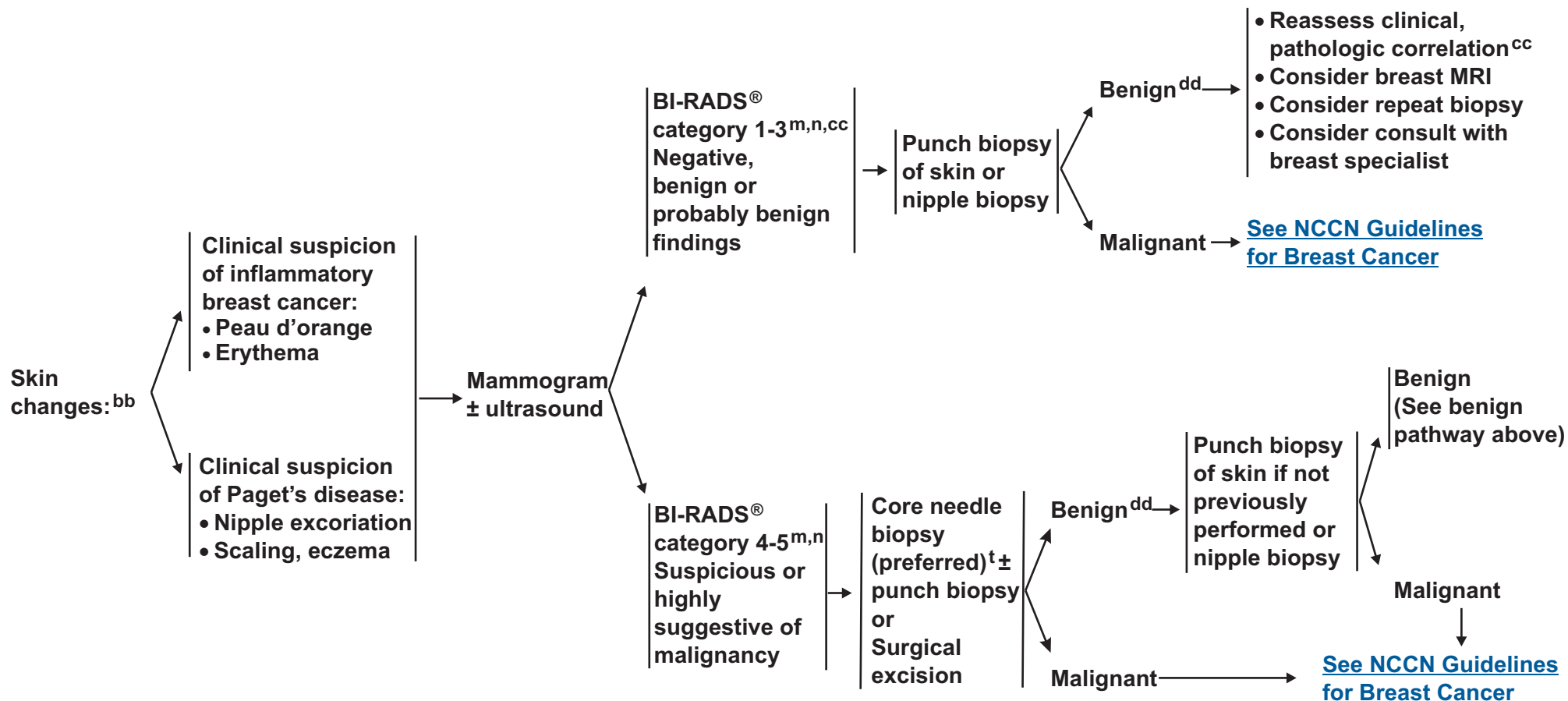
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PRESENTING SIGNS/ SYMPTOMS

DIAGNOSTIC FOLLOW-UP



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[†] 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.

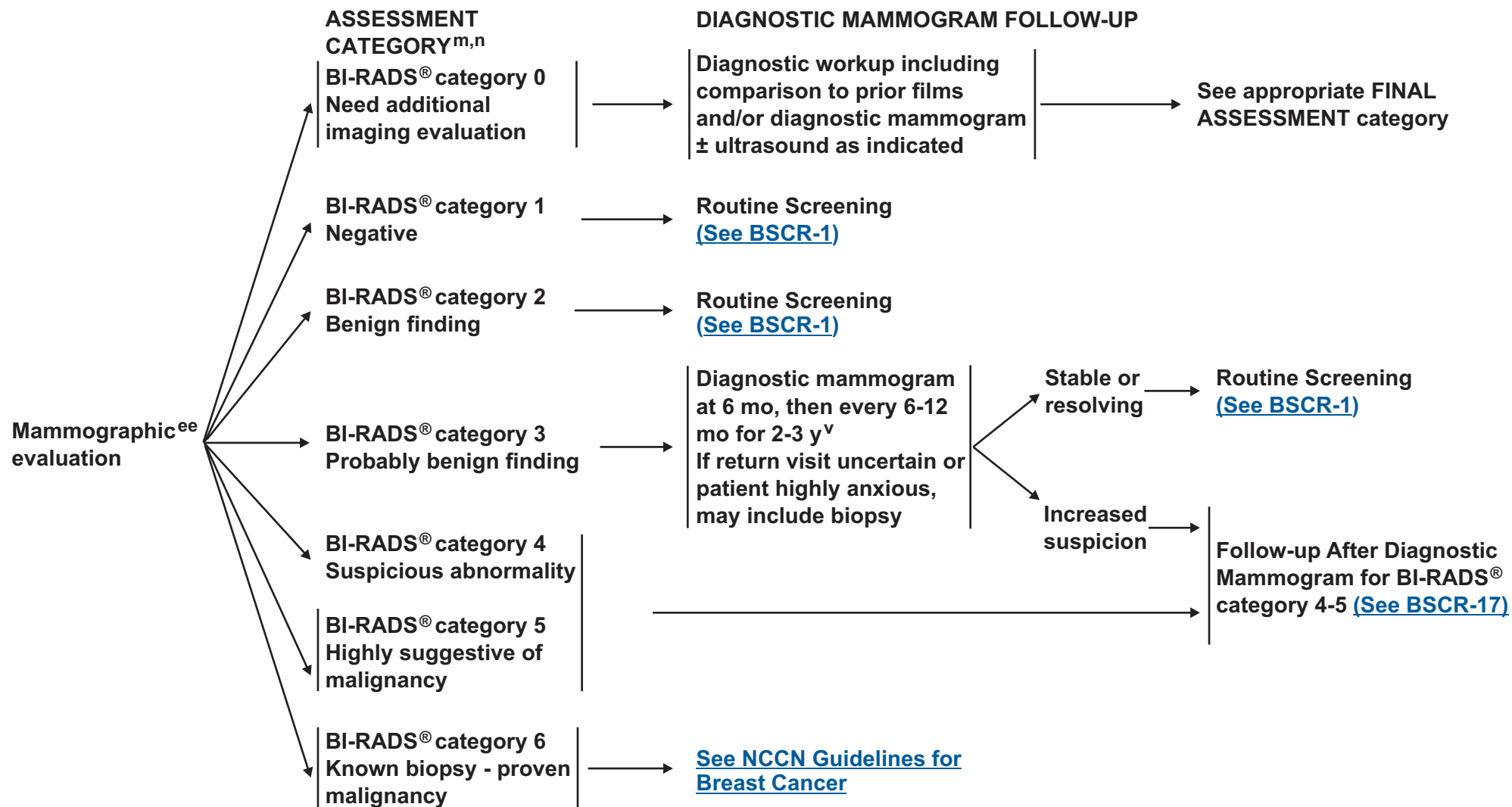
^{bb} This may represent serious disease of the breast and needs evaluation.

^{cc} If clinically of low suspicion, 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.

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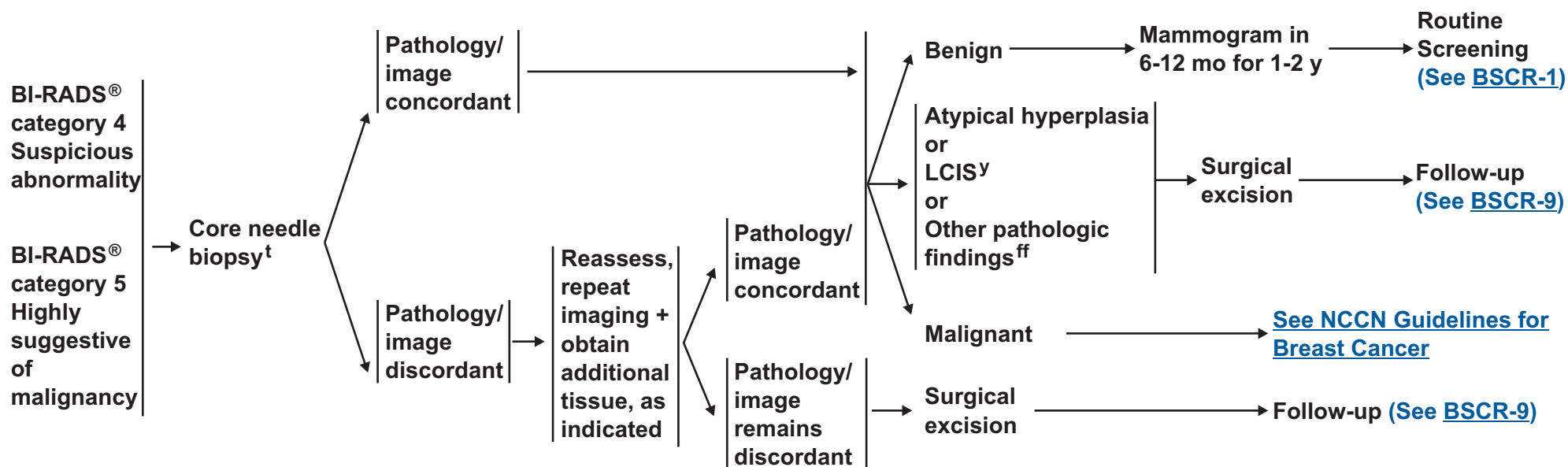
^vThere may be variability on the follow-up interval based on the level of suspicion.

^{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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ASSESSMENT FOLLOW-UP AFTER DIAGNOSTIC MAMMOGRAM CATEGORY^{m,n}



^mSee Assessment Category Definitions (BSCR-C).

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^tFNA 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.

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

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

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BREAST SCREENING CONSIDERATIONS

- Women should be counseled regarding potential benefits, risks, and limitations of breast screening.
- Thorough clinical breast exam involves inspection and palpation of all breast tissue including lymph node basins.
- Consider severe comorbid conditions limiting life expectancy and whether therapeutic interventions are planned.
- Upper age limit for screening is not yet established.
- Current evidence does not support the routine use of breast scintigraphy (eg, sestamibi scan) or ductal lavage as screening procedures.
- There are several studies supporting the use of ultrasound for breast cancer screening as an adjunct to mammography for high-risk women with dense breast tissue.¹
- Digital mammography appears to benefit young women and women with dense breasts.²
- 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.
- Early studies show promise for tomosynthesis mammography. Currently, there is insufficient evidence to recommend routine use for screening or diagnosis at this time.

RECOMMENDATIONS FOR BREAST MRI SCREENING AS AN ADJUNCT TO MAMMOGRAPHY³

Recommend Annual MRI Screening (Based on Evidence):⁴

- BRCA mutation
- First-degree relative of BRCA carrier, but untested
- Lifetime risk ~20% or greater, as defined by BRCAPRO or other models that are largely dependent on family history ([See BSCR-2](#))

Recommend Annual MRI Screening (Based on Expert Consensus Opinion):⁵

- Radiation to chest between age 10 and 30 years
- Li-Fraumeni syndrome⁶ and first-degree relatives
- Cowden and Bannayan-Riley-Ruvalcaba syndromes⁶ and first-degree relatives

Insufficient Evidence to Recommend for or Against MRI Screening:⁷

- Lifetime risk 15%–20%, as defined by BRCAPRO or other models that are largely dependent on family history
- LCIS or atypical lobular hyperplasia (ALH)
- Atypical ductal hyperplasia (ADH)
- Heterogeneously or extremely dense breast on mammography
- Women with a personal history of breast cancer,⁸ including ductal carcinoma in situ (DCIS)

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

- Women at <15% lifetime risk

[See footnotes on BSCR-A 2 of 2](#)

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BREAST SCREENING CONSIDERATIONS

- 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.
- ³Breast 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.
- ⁴Evidence from nonrandomized screening trials and observational studies.
- ⁵Based on evidence of lifetime risk for breast cancer.
- ⁶There is variation in recommendations for initiation of screening for different genetic syndromes. [See NCCN Guidelines for Genetic/Familial High-Risk Assessment.](#)
- ⁷Payment 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.
- ⁸Brennan S, Liberman L, Dershaw DD, et al. Breast MRI screening of women with a personal history of breast cancer. *AJR* 2010;195:510-516.

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.

RISK FACTORS USED IN THE MODIFIED GAIL MODEL¹

- 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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NCCN Guidelines Version 2.2013 Breast Cancer Screening and Diagnosis

MAMMOGRAPHIC ASSESSMENT CATEGORY DEFINITIONS^{1,2}

BI-RADS® - MAMMOGRAPHY FINDINGS

A. Assessment Is Incomplete:

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

Finding for which additional evaluation is needed. This is almost always used in a screening situation. Under certain circumstances this category may be used after a full mammographic workup. A recommendation for additional imaging evaluation may include, but is not limited to spot compression, magnification, special mammographic views, and ultrasound. Whenever possible, if the study is not negative and does not contain a typically benign finding, the current examination should be compared to previous studies. The radiologist should use judgment on how vigorously to attempt obtaining previous studies. Category 0 should only be used for old film comparison when such comparison is required to make a final assessment.

B. Assessment Is Complete - Final Assessment Categories:

Category 1: Negative:

There is nothing to comment on. The breasts are symmetric and no masses, architectural distortion, or suspicious calcifications are present.

Category 2: Benign Finding(s):

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, multiple secretory calcifications, and fat-containing lesions such as oil cysts, lipomas, galactoceles, and mixed-density hamartomas all have characteristically benign appearances, and may be labeled 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.

Note that both Category 1 and Category 2 assessments indicate that there is no mammographic evidence of malignancy. 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.

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®--4th Edition. ACR Breast Imaging Reporting and Data System, Breast Imaging Atlas; BI-RADS. Reston VA. American College of Radiology, 2003. For more information, see www.acr.org.

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MAMMOGRAPHIC ASSESSMENT CATEGORY DEFINITIONS^{1,2}

BI-RADS® - MAMMOGRAPHY FINDINGS

Category 3: Probably Benign Finding - Short Interval Follow-Up Suggested:

A finding placed in this category should have less than a 2% risk of malignancy. It is not expected to change over the follow-up interval, but the radiologist would prefer to establish its stability.

There are several prospective clinical studies demonstrating the safety and efficacy of initial short-term follow-up for specific mammographic findings.

Three specific findings are described as being probably benign (the noncalcified mass, the focal asymmetry, and the cluster of round [punctate] calcifications; the latter is anecdotally considered by some radiologists to be an absolutely benign feature). All the published studies emphasize the need to conduct a complete diagnostic imaging evaluation before making a probably benign (Category 3) assessment; hence, it is inadvisable to render such an assessment when interpreting a screening examination. Also, all the published studies exclude palpable lesions, so the use of a probably benign assessment for a palpable lesion is not supported by scientific data. Finally, evidence from all published studies indicate the need for biopsy rather than continued follow-up when most probably benign findings increase in size or extent.

While the vast majority of findings in this category will be managed with an initial short-term follow-up (6 mo) examination followed by additional examinations until longer-term (2 y or longer) stability is demonstrated, there may be occasions where biopsy is done (patient wishes or clinical concerns).

Category 4: Suspicious Abnormality - Biopsy Should Be Considered:

This category is reserved for findings that do not have the classic appearance of malignancy but have a wide range of probability of malignancy that is greater than those in Category 3. Thus, most recommendations of breast interventional procedures will be placed within this category. It is encouraged that the relevant probabilities be indicated so the patient and her physician can make an informed decision on the ultimate course of action.

Category 5: Highly Suggestive of Malignancy - Appropriate Action Should Be Taken:

These lesions have a high probability ($\geq 95\%$) of being cancer. This category contains lesions for which one-stage surgical treatment could be considered without preliminary biopsy. However, current oncologic management may require percutaneous tissue sampling as, for example, when sentinel node imaging is included in surgical treatment or when neoadjuvant chemotherapy is administered at the outset.

Category 6: Known Biopsy - Proven Malignancy - Appropriate Action Should Be Taken:

This category is reserved for lesions identified on the imaging study with biopsy proof of malignancy prior to definitive therapy.

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®--4th Edition. ACR Breast Imaging Reporting and Data System, Breast Imaging Atlas; BI-RADS. Reston VA. American College of Radiology, 2003. For more information, see www.acr.org.

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ULTRASOUND ASSESSMENT CATEGORY DEFINITIONS^{1,2}

BI-RADS® - ULTRASOUND FINDINGS

A. Assessment is Incomplete:

Category 0 - Need Additional Imaging Evaluation:

In many instances, the ultrasound examination completes the evaluation of the patient. If ultrasound is the initial study, other examinations may be indicated. An example would be the need for mammography if ultrasound were the initial study for a patient in her late 20s evaluated with ultrasound for a palpable mass that had suspicious sonographic features. Another example might be where mammography and ultrasound are nonspecific, such as differentiating between scarring and recurrence in a patient with breast cancer treated with lumpectomy and radiation therapy. Here, MRI might be the recommendation. A need for previous studies to determine appropriate management might also defer a final assessment.

B. Assessment is Complete — Final Categories:

Category 1: Negative:

This category is for sonograms with no abnormality, such as a mass, architectural distortion, thickening of the skin, or microcalcifications. For greater confidence in rendering a negative interpretation, an attempt should be made to correlate the ultrasound and mammographic patterns of breast tissue in the area of concern.

Category 2: Benign Finding(s):

Essentially a report that is negative for malignancy. Simple cysts would be placed in this category, along with intramammary lymph nodes (also possible to include in Category 1), breast implants, stable postsurgical changes, and probable fibroadenomas noted to be unchanged on successive ultrasound studies.

Category 3: Probably Benign Finding - Short-interval Follow-Up Suggested:

With accumulating clinical experience and by extension from mammography, a solid mass with circumscribed margins, oval shape, and horizontal orientation, most likely a fibroadenoma, should have a <2% risk of malignancy. Although additional multicenter data may confirm safety of follow-up rather than biopsy based on ultrasound findings, short-interval follow-up is currently increasing as a management strategy. Nonpalpable complicated cysts and clustered microcysts might also be placed in this category for short-interval follow-up.

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

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ULTRASOUND ASSESSMENT CATEGORY DEFINITIONS^{1,2}

BI-RADS® - ULTRASOUND FINDINGS

Category 4: Suspicious Abnormality—Biopsy Should Be Considered:

Lesions in this category would have an intermediate probability of cancer, ranging from 3% to 94%. An option would be to stratify these lesions, giving them a low, intermediate, or moderate likelihood of malignancy. In general, Category 4 lesions require tissue sampling. Needle biopsy can provide a cytologic or histologic diagnosis. Included in this group are sonographic findings of a solid mass without all of the criteria for a fibroadenoma and other probably benign lesions.

Category 5: Highly Suggestive of Malignancy—Appropriate Action Should Be Taken:

(Almost certainly malignant)

The abnormality identified sonographically and placed in this category should have a 95% or higher risk of malignancy so that definitive treatment might be considered at the outset. With the increasing use of sentinel node imaging as a way of assessing nodal metastases and also with the increasing use of neoadjuvant chemotherapy for large malignant masses or those that are poorly differentiated, percutaneous sampling, most often with imaging-guided core needle biopsy, can provide the histopathologic diagnosis.

Category 6: Known Biopsy-Proven Malignancy—Appropriate Action Should Be Taken:

This category is reserved for lesions with biopsy proof of malignancy prior to institution of therapy, including neoadjuvant chemotherapy, surgical excision, or mastectomy.

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®--4th Edition. ACR Breast Imaging Reporting and Data System, Breast Imaging Atlas; BI-RADS. Reston VA. American College of Radiology, 2003. For more information, see www.acr.org.

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Discussion

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 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



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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



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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.



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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.



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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



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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



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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



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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.
<p>Non-simple cyst</p> <ul style="list-style-type: none"> • complicated • complex 	<p>Has one or more characteristics not found in a simple cyst.</p> <p>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.</p> <p>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.</p>
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