Cancer Statistics: Breast Cancer In Situ

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An estimated 60,290 new cases of breast carcinoma in situ are expected to be diagnosed in 2015, and approximately 1 in 33 women is likely to receive an in situ breast cancer diagnosis in her lifetime. Although in situ breast cancers are relatively common, their clinical significance and optimal treatment are topics of uncertainty and concern for both patients and clinicians. In this article, the American Cancer Society provides information about occurrence and treatment patterns for the 2 major subtypes of in situ breast cancer in the United States—ductal carcinoma in situ and lobular carcinoma in situ—using data from the North American Association of Central Cancer Registries and the 13 oldest Surveillance, Epidemiology, and End Results registries. The authors also present an overview of in situ breast cancer detection, treatment, risk factors, and prevention and discuss research needs and initiatives. CA Cancer J Clin 2015;65:481-495. © 2015 American Cancer Society.

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Introduction
Excluding skin cancers, invasive breast cancer is the most common cancer diagnosed among women in the United States, with an estimated 231,840 new cases expected to be diagnosed in 2015. These statistics do not include 60,290 new cases of breast carcinoma in situ. Although about 1 in 33 women is likely to receive an in situ breast cancer diagnosis in her lifetime, the clinical significance of a breast carcinoma in situ diagnosis and optimal approaches to treatment are topics of uncertainty and concern for both patients and clinicians.1-3

The term breast carcinoma in situ was coined long ago to describe lesions comprised of abnormal epithelial cells that are completely confined within breast lobules and/or ducts but that look very similar to cells of invasive carcinoma when viewed under a microscope. For many years, it was assumed that these cells were potentially able to invade the adjacent mammary stroma and that, in the absence of treatment, they would eventually progress to invasive cancer. However, it is now understood that in situ breast cancers lack or incompletely express several of the hallmarks of invasive cancers4 and that the molecular changes involved in progression to invasive cancer do not always occur. Among the 2 major types of breast carcinoma in situ, ductal carcinoma in situ (DCIS) is considered a true (nonobligatory) cancer precursor, and its treatment is often similar to that for small, lymph node-negative breast cancer; whereas lobular carcinoma in situ (LCIS), which is also known as lobular neoplasia, is primarily viewed as an indicator of increased breast cancer risk. This article will provide up-to-date information on risk factors, occurrence, and treatment patterns in the United States, with an overview of clinical and treatment information as background for readers whose practice or research does not focus on these diseases.

Materials and Methods
We used 2 sources for breast carcinoma in situ incidence data in this report. Data on patients diagnosed during 2007 through 2011 were obtained from the North American Association of Central Cancer Registries (NAACCR) for analyses of incidence rates by race/ethnicity and age and for the distribution of prognostic characteristics among DCIS cases.5 Incidence data from NAACCR included data from all US states and the District of Columbia except Arkansas, Minnesota, and Nevada.

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Delay-adjusted incidence rates from the 13 oldest Surveillance, Epidemiology, and End Results (SEER) registries, representing approximately 14% of the US population, were used for analyses of incidence trends from 1992 to 2011. Incidence rates and case distributions were calculated using SEER\textsuperscript{*}Stat software (version 8.2.1).\textsuperscript{7} We analyzed trends in DCIS and LCIS incidence rates using Joinpoint software (version 4.1.1.3) which involved fitting a series of joined straight lines on a logarithmic scale to the trends in annual rates.\textsuperscript{8,9} Incidence rates are presented per 100,000 women and are age-adjusted to the 2000 US standard population to allow comparisons across populations with different age distributions. Analyses in this report are restricted to carcinoma in situ of the breast in women because of the rarity of this diagnosis in men; in 2011, there were only 259 men with breast carcinoma in situ in NAACCR data (all US states except Arkansas, Minnesota, and Nevada); 90% were DCIS, and 7% were LCIS.\textsuperscript{5}

Age-specific and race/ethnicity-specific incidence rates for DCIS and LCIS, surgical treatment patterns, and prognostic characteristics of DCIS subtypes (tissue architectural patterns) were based on cases reported to NAACCR during 2007 through 2011 after exclusion of data from 7 states based on lack of consent (Kansas, Maryland, New Hampshire, and Vermont), lack of inclusion in the NAACCR data (Minnesota), and failure to achieve certification of high-quality data by NAACCR during one or more of the years under study (Arkansas and Nevada). Female patients aged 20 years and older with a first primary, microscopically confirmed diagnosis of DCIS between 2007 and 2011 were selected. DCIS was defined using the following \textit{International Classification of Diseases for Oncology, Third Edition} (ICD-O-3) codes: 8201, 8230, 8500 through 8507, 8523; and, for LCIS, the codes 8520 and 8524 were used.\textsuperscript{10} ICD-O-3 codes were also used to categorize DCIS cases by subtype (DCIS, not otherwise specified [8500, 8523], comedocarcinoma [8501], papillary [8503], micropapillary [8507], cribriform [8201], solid [8230], and other [8502, 8504-8506]) based on a scheme used previously.\textsuperscript{11} DCIS grade is classified by pathologists in 3 categories (grades I, II and III); where grade IV was coded in a registry record, it was assumed to be grade III. Patients who were reported only from a nursing home/convalescent center, autopsy, or death certificate were excluded.

Multinomial logistic regression was used to assess the association between DCIS treatment course and the following predictors: age (20-39, 40-49, 50-59, 60-69, 70-79, and ≥80 years), race/ethnicity, year of diagnosis, insurance status, tumor size, histology subgroup, tumor (nuclear) grade, and census region. Additional exclusions were made in the data set used for these analyses. Patients from Massachusetts (2007-2011), Texas (2007-2010), and Pennsylvania (2011) were excluded, because ≥20% of women were missing radiation treatment data. Patients who did not have surgical treatment (n = 5030); who underwent surgical procedures other than breast-conserving surgery (BCS), unilateral mastectomy, or bilateral mastectomy (n = 534); with unknown receipt of surgical procedures (n = 534); who had missing data regarding radiation treatment (n = 2430); and who had missing data on prognostic factors, including tumor size and grade (n = 56,172), were also excluded. Differences in the distribution of baseline characteristics between women who received different treatments were evaluated using chi-square tests with a significance level at .05 (2-sided).

\textbf{Background}

\textbf{DCIS}

The vast majority (83%) of newly diagnosed in situ breast cancers are DCIS. DCIS refers to a condition in which abnormal cells arising in the terminal duct lobular units replace the epithelium of terminal and subsegmental ducts and sometimes the acini as well; however, the basement membrane remains intact, with no evidence of stromal invasion. Criteria for the diagnosis of DCIS and its various subtypes take into account the degree of cytologic abnormality, the architectural patterns formed by the abnormal cells, the presence or absence of necrosis (cellular death and degeneration), and a minimum required size (measured diameter or number of involved ducts) of the lesion (although the details of how these features are applied to individual cases are beyond the scope of this review).\textsuperscript{12}

DCIS is viewed as a true (nonobligatory) precursor lesion for invasive cancer; however, data are limited about the proportion of detected DCIS lesions that will progress to invasive cancer without treatment. Long-term studies of women whose DCIS was untreated because the biopsy was misclassified as benign found that 20% to 53% were diagnosed with an invasive breast cancer over the course of 10 or more years.\textsuperscript{13-17} A recent update of one of those studies\textsuperscript{18} reported follow-up on 45 women with low-grade DCIS who were treated by biopsy only and were recognized retrospectively during a larger review of surgical pathology diagnoses and original histological slides for 26,539 consecutive breast biopsies performed at Vanderbilt, Baptist, and Saint Thomas Hospitals in Nashville, Tennessee, from 1950 to 1989, including 28 women whose long-term follow-up was reported previously. Sixteen women (36%) developed invasive breast carcinoma, all in the same breast and quadrant as their incident DCIS. Eleven of these invasive breast carcinomas were diagnosed within 10 years of the DCIS biopsy. Subsequent cases were diagnosed at 12, 23, 25, 29, and 42 years. Seven women, including one who developed invasive breast cancer 29 years after her DCIS biopsy, developed distant metastases,
resulting in death from 1 to 7 years postdiagnosis of invasive breast carcinoma.

The relevance of historical studies to the natural history of more contemporary lesions should be interpreted with caution, as characteristics of contemporary DCIS lesions differ from those of DCIS lesions diagnosed before mammographic screening was widespread, and, in some studies, the extent of resection is unclear. Additional insight into the behavior of small DCIS lesions treated with excision alone comes from a multicenter intergroup trial that was open to patients who were diagnosed during 1997 through 2002 with low-grade or intermediate-grade DCIS >0.3 cm and <2.5 cm in size (n = 565) or with high-grade DCIS >0.3 cm and <1.0 cm in size (n = 105) in which all lesions were completely excised with margins of at least 3 mm, and had negative postexcision mammograms. With a median follow-up period of 6.3 years, the 7-year rates of local recurrence were 10.5% for the low-grade/intermediate-grade group and 18% for the high-grade DCIS group, with invasive carcinoma comprising 53% of recurrences in the low-grade/intermediate-grade group and 35% of recurrences in the high-grade group. In a subset of 327 patients, 10-year rates of invasive cancer recurrence were 3.7%, 12.3%, and 19.2% in the low-grade, intermediate-grade, and high-grade groups, respectively.1,19

Although DCIS can present as a palpable mass, it is most often detected by the appearance of microcalcifications in a mammogram. The histologic diagnosis of DCIS is commonly made by examination of core-needle biopsy, followed by excision and definitive pathologic examination. Approximately 25% of lesions diagnosed as DCIS on core biopsy will be found to also include invasive carcinoma after surgical resection; factors associated with the finding of invasive cancer include larger lesion size, intermediate or high nuclear grade, and negative hormone receptor status.20,21

Because of the potential for finding invasive disease, the National Comprehensive Cancer Network (NCCN) guidelines recommend that sentinel lymph nodal biopsy (SLNB) be considered for patients to be treated with mastectomy or with excision in an anatomic location (eg, tail of the breast) that could compromise the performance of a future sentinel lymph node biopsy.22

The identification of foci of invasion within a lesion consisting largely of DCIS is influenced by the proportion of excised tissue that is examined microscopically. There is good interrater reliability among pathologists in agreeing whether or not the microscopic images they are viewing indicate invasion. Atypical ductal hyperplasia (ADH), like DCIS, is an intraductal proliferation of abnormal cells, but the two are distinguished based on criteria involving the degree of cytologic abnormality and the size of the lesion.12

Interobserver reliability is somewhat lower for distinguishing DCIS from ADH (compared with distinguishing DCIS with or without invasion), although there has been variation among studies quantifying this issue, due in part to differences in methodological points, such as selection of cases and specification of standardized diagnostic criteria.23-25

Prognostic and predictive factors for local in situ or invasive recurrence that are measured for DCIS include nuclear grade, histologic type, size, estrogen receptor (ER) status, margin status, and distance from nearest margin.26 Nuclear grade for DCIS is classified based on 6 morphologic features described in Table 1.27

DCIS is classified based on architectural pattern (the term used by clinicians), and more than one pattern may be present. Registries refer to these patterns as histologic type or histology as a matter of consistency with the classification of all other neoplasms. Because these registries are the source of data reported in this review, we refer to DCIS architectural patterns as histologic types. DCIS is generally classified as papillary, solid, comedo, micropapillary, or cribriform.27 Comedo DCIS typically has a higher nuclear grade and a higher proliferation rate than noncomedo DCIS.28 Although not captured by cancer registries, the pathology

### TABLE 1. Nuclear Grade of Ductal Carcinoma In Situ

| FEATURE          | GRADE I (LOW)                      | GRADE II (INTERMEDIATE) | GRADE III (HIGH) |
|------------------|-----------------------------------|-------------------------|------------------|
| Orientation      | Polarized toward luminal spaces    | Intermediate            | Markedly pleomorphic |
| Pleomorphism     | Monotonous (monomorphic)          | Intermediate            | Markedly pleomorphic |
| Chromatin        | Usually diffuse, finely dispersed | Intermediate            | Usually vesicular with irregular chromatin distribution |
| Nucleoli         | Only occasional                    | Intermediate            | Prominent, often multiple |
| Mitoses          | Only occasional                    | Intermediate            | May be frequent   |
| Size             | From 1.5 to 2 times the size of a  | Intermediate            | Greater than 2 times the size of a normal RBC or a normal duct epithelial cell nucleus |
| RBC indicates red blood cell. |

Source: College of American Pathologists. Protocol for the Examination of Specimens From Patients With Ductal Carcinoma in Situ (DCIS) of the Breast. Version 3.2.0.0.27

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report usually describes the degree of necrosis and microscopically visible calcification, which is correlated with the finding of mammographic calcifications. In central or comedo necrosis, the central portion of an involved ductal space is replaced by an area of extensive necrosis that is easily detected at low magnification. In contrast, punctate necrosis describes either small foci of necrosis, which are indistinct at low magnification, or single-cell necrosis. Although central necrosis is typically associated with high-grade nuclei (as in the comedo DCIS subtype), it can also occur with DCIS of low or intermediate grade.

Size of the DCIS lesion is also a prognostic factor associated with recurrence. Size may be difficult to measure, because DCIS often involves the ductal system in a complex, 3-dimensional branching pattern. Positive or close surgical margins are associated with a higher risk of recurrence, and some women who undergo BCS require reexcision to achieve clear margins.\(^{20,22,29}\) In addition to having prognostic significance, ER status is important because tamoxifen therapy is an option for women with ER-positive tumors to decrease the risk of recurrence or to prevent second primary breast cancers from developing.

Treatment for DCIS usually involves either BCS with radiation therapy (RT) or mastectomy. RT is recommended for most women who have BCS, because randomized trials show strong and consistent evidence that RT after BCS approximately halves the rate of recurrence in the affected breast. A meta-analysis of 4 clinical trials that included a total of 3925 women with DCIS found that, at 5 years after treatment, 18% of women who had BCS without RT experienced a recurrence compared with 8% of women who had BCS plus RT.\(^{30}\) At 10 years of follow-up, 28% of women who received BCS without RT had experienced a recurrence compared with 13% of women who received BCS plus RT.\(^{30}\) In both treatment groups, about half of the recurrences were DCIS, and half were invasive breast cancer. Updated evidence from these clinical trials was summarized in 2014 by Recht, who found that rates of local failure at median follow-up intervals of approximately 13 to 17 years were 25% to 35% in the unirradiated arms compared with 10% to 20% in the irradiated arms.\(^{31-35}\) A more recent prospective randomized trial (Radiation Therapy Oncology Group trial 9804; 1998-2006) involving 636 women with mammographically detected, good-risk DCIS (low-grade or intermediate-grade DCIS >0.3 cm and <2.5 cm in size) found that, at median follow-up of 7.7 years, the 7-year failure rate was 0.9% in the RT arm and 6.7% in the observation arm. The histology of the localized failures in the observation arm was invasive in 42.1% and noninvasive in 57.9% of patients; in the RT arm, there were only 2 localized failures, one patient each experienced invasive and noninvasive localized failure. Approximately 62% of women in that trial received tamoxifen therapy.\(^{36}\)

Although RT has been shown to reduce the risk of recurrence among DCIS patients, it also has some drawbacks and risks. These include the patient burden of daily treatment for 6 weeks and short-term side effects, such as fatigue and skin toxicity, as well as a slightly increased risk of secondary cancers.\(^{37,38}\) An additional drawback of RT is that, once a woman has received it after BCS for DCIS, she cannot receive it again in the ipsilateral breast should an invasive cancer develop. The NCCN treatment guidelines suggest that BCS followed by observation is a reasonable option for some women with low-risk disease.\(^{22}\)

Mastectomy is considered an acceptable option for treatment of DCIS and is the recommended therapy for some women, including patients with extensive and/or multifocal DCIS, those with a large tumor-to-breast-tissue ratio, those who should not receive radiation because of certain medical conditions or who have received prior RT, and those for whom negative margins could not be achieved with BCS.\(^{39}\) Women who have a mastectomy for DCIS have a very low probability of local recurrence but remain at increased risk of developing DCIS or invasive breast cancer in the contralateral breast.\(^{40}\) In addition to being followed by clinical breast examination and mammography, magnetic resonance imaging (MRI) of the contralateral breast may also be recommended for some women with a history of DCIS who are at high risk because of certain other risk factors.\(^{41}\)

Some women with unilateral DCIS choose to have bilateral mastectomy to prevent cancer in the unaffected breast.\(^{42}\) Studies suggest that the decision to have a bilateral mastectomy may be influenced by the presence of other breast cancer risk factors, including a family history, whereas other women may make this decision based primarily on concern about future breast cancer risk.\(^{43}\)

Women who undergo mastectomy for treatment of DCIS may also elect to have breast reconstruction. In a population-based study of 2428 DCIS patients in southern California who were treated with mastectomy between 2003 and 2007, 1118 (46%) had immediate reconstruction, with higher use of reconstruction among younger women, non-Hispanic (NH) white women, and privately insured women.\(^{44}\)

For women with ER-positive DCIS, hormone therapy with tamoxifen is associated with a significantly decreased risk of future breast events, including invasive cancer and DCIS in either breast.\(^{33,45,46}\) NCCN guidelines recommend tamoxifen for women with ER-positive DCIS treated with BCS and RT to reduce the risk of recurrence or invasive cancer in the ipsilateral breast.\(^{47}\) Women with DCIS treated with unilateral mastectomy may also be offered tamoxifen to reduce their risk of cancer in the contralateral breast.\(^{48}\) In either situation, the use of tamoxifen would be...
contraindicated by a history of deep vein thrombosis, pulmonary embolism, or uterine cancer. Clinical trials are currently evaluating aromatase inhibitors as an alternative to tamoxifen therapy in postmenopausal women with DCIS. A recent presentation from one of these studies reported decreased total breast cancer events and lower rates of invasive cancer at 10 years among women who received anastrozole compared with tamoxifen; this benefit was observed primarily in women younger than age 60 years.\(^1\)

The University of Southern California/Van Nuys Prognostic Index, which takes into account tumor size, margins, grade, presence of necrosis, and age, may be used to guide treatment decisions. A nomogram has also been published that estimates the probability of 5-year and 10-year ipsilateral breast tumor recurrences after BCS based on 10 factors (age at diagnosis, family history, initial presentation, radiation, adjuvant endocrine therapy, nuclear grade, necrosis, margins, number of excisions, and year of surgery).\(^5\)

More recently, studies have found that a 12-gene assay performed on tumor tissue, the Oncotype DX DCIS Score (Genomic Health, Redwood City, Calif), can predict the risk of local recurrence at 10 years in women treated with BCS without RT. This assay, which is discussed in more detail below, is used by some clinicians to identify women who may be able to forgo RT.\(^5\)

NCCN guidelines for follow-up for patients with DCIS include interval history and physical examination every 6 to 12 months for 5 years, then annually; mammogram every 12 months (and 6–12 months post-RT if the breast is conserved [category 2B]); and, if treated with tamoxifen, monitoring per NCCN guidelines.\(^2\)

**LCIS**

LCIS refers to a monomorphic population of dyshesive cells filling and distending the terminal duct lobular units. LCIS frequently occurs in conjunction with atypical lobular hyperplasia (ALH), and the term “lobular neoplasia” is sometimes used to refer to both ALH and LCIS. The distinction between ALH and LCIS is made based on the percentage of acini in the affected terminal duct lobular unit distended by lobular proliferation (<50% for ALH and >50% for LCIS) and whether the abnormal cells completely fill at least one lobular unit.\(^1\)

Pleomorphic LCIS, a variant of LCIS in which the cells have a greater degree of nuclear pleomorphism and usually contain abundant cytoplasm, shows the characteristic molecular changes of classical lobular neoplasia as well as additional molecular changes, including human epidermal growth factor receptor 2 (HER2) amplification, which raise concern that it might have a different clinical outcome than classic LCIS. Pleomorphic LCIS is often found in association with invasive breast cancer.\(^1\) Both pleomorphic LCIS and classic LCIS can be associated with comedo necrosis and calcifications and may be difficult to distinguish from DCIS based on the appearance of routinely stained tissue preparations alone. E-cadherin staining is useful in the diagnosis of LCIS because loss of this transmembrane protein (which, when present, mediates cell adhesion) is a very common characteristic of LCIS.\(^5\)

LCIS is primarily viewed as a marker for increased risk of developing invasive breast cancer and not a precursor of invasive cancer. The strongest evidence that LCIS is more of a risk indicator than a direct cancer precursor comes from registry-based studies. One study of women diagnosed with LCIS from 1973 to 1998 and treated with BCS found that 7% of women developed invasive breast cancer within 10 years, with the increased risk of invasive disease equally distributed between both breasts.\(^6\) Thus, rather than an emphasis on local treatment, such as BCS plus RT, as is recommended for DCIS patients, care for women with LCIS emphasizes medical surveillance and risk-reduction strategies for both breasts. However, there is increasing evidence that LCIS may also act as a nonobligate precursor in the progression to invasive carcinoma.\(^5\)

Pure LCIS is not typically associated with clinical findings, such as a lump or mammographic abnormality (microcalcifications); thus, it is most often diagnosed incidentally during a breast biopsy performed for another indication. Although the entire suspicious area is often removed as part of the diagnostic workup to rule out the presence of DCIS or invasive cancer, complete removal with adequate margins is generally considered unnecessary.\(^5\) There is some debate about whether an excisional biopsy is indicated for all women diagnosed with LCIS on core biopsy.\(^2\) The most recent NCCN guidelines panel recommended that, “for LCIS of the usual type (<4 terminal duct lobular units found in a single core) found on core biopsy as a result of routine screening for calcifications and without imaging discordance may be managed by imaging follow-up.”\(^2\)

Although some guidelines recommend treating pleomorphic LCIS as a cancer precursor, with complete removal with negative margins, the available literature is too limited to consider this an evidence-based recommendation.\(^2\)

Guidelines do not recommend unilateral mastectomy as a standard treatment for usual-type LCIS because of evidence that the risk of breast cancer subsequent to an LCIS diagnosis is equal for both breasts. Bilateral mastectomy may be considered as a risk-reduction strategy, especially for women with LCIS and a strong family history of breast cancer. Medical surveillance recommendations from the NCCN include annual mammography and clinical breast examination every 6 to 12 months from the time of diagnosis for women with LCIS.\(^4\) Although the lifetime risk of invasive breast cancer for a woman with LCIS may exceed 20% (depending on her age at diagnosis), the American Cancer Society guidelines do not support routine use of
magnetic resonance imaging screening for surveillance of women with LCIS, because the evidence for its effectiveness as an addition to mammography has not been demonstrated in this population.41 Both the American Society of Clinical Oncology and the NCCN recommend discussing chemoprevention therapy with LCIS patients; tamoxifen is the only option for premenopausal women, and tamoxifen or raloxifene may be recommended for postmenopausal women, depending on other health conditions.47,49 The American Society of Clinical Oncology also lists exemestane as an option in postmenopausal women; however, this is not a US Food and Drug Administration-approved indication for this drug.49

Risk Factors for In Situ Breast Cancer

There is less information available about the risk factors for in situ than for invasive breast cancers, as many epidemiologic studies of breast cancer risk factors either exclude or have very small numbers of women with in situ cancers. Although much of the information about epidemiologic risk factors for in situ cancers relates to DCIS, this review will mention risk factors for LCIS where any information is known.

Nonmodifiable risk factors for DCIS and LCIS include family history and genetic predisposition, mammographic breast density, and a history of ADH or ALH. In one study, both DCIS and LCIS patients were significantly more likely to report a first-degree family history of breast cancer than controls with no history of invasive or in situ breast disease (odds ratio [OR], 1.6; 95% confidence interval [CI], 1.3–2.1 and OR, 1.8; 95% CI, 1.2–2.9, respectively).63 Another case-control study investigated genetic polymorphisms associated with breast and other cancers among women with invasive lobular cancer (ILC) (with or without LCIS) and those with LCIS only and found that many of the single nucleotide polymorphisms (SNPs) that predispose to ILC also predispose to LCIS.64 Similarly, a study that compared 12 SNPs previously associated with breast cancer among women with invasive ductal cancer (IDC) and DCIS versus controls found that there was only one SNP in which there was a statistically significant difference in the OR for IDC and LCIS.65

High mammographic breast density is an important risk factor for invasive breast cancer and may also increase risk for DCIS. A pooled analysis of 6 studies including over 10,000 women found that the association between breast density and DCIS risk was strongest for women younger than 55 years.66 In this age group, women who had high mammographic density had about a 2-fold increased risk for DCIS compared with women who had lower breast density. For women ages 55 to 64 years, high mammographic density was associated with a 1.5-fold increased risk.

Breast density is also a risk factor for the development of contralateral breast cancer after DCIS treatment. In one prospective study of women treated with BCS for DCIS between 1993 and 2005, the hazard ratio (HR) for the development of invasive breast cancer in the contralateral breast for women who had medium to high breast density (Breast Imaging-Reporting and Data System categories 3 and 4), compared with women who had low and average breast density (Breast Imaging-Reporting and Data System categories 1 and 2), was 3.1 (95% CI, 1.6–6.1).67

Long-term follow-up studies of women diagnosed with ADH and ALH find that they have about a 4-fold increased risk for breast cancer (invasive or in situ), but those studies do not calculate relative risks for in situ cancers separately.68,69

One recent large study of 1.2 million postmenopausal women living in the United Kingdom investigated risk factors for IDC and DCIS.65 The risk of DCIS was higher for women who had fewer or no children, those who were older at the time of first birth, or those who reached menopause after age 50 years. DCIS incidence was not associated with age at menarche in that study; but, unlike many other studies, researchers also found no associations between earlier age at menarche and invasive breast cancer risk. With respect to nonreproductive risk factors, the study found no association between DCIS and age, body mass index, or alcohol consumption; but risk was increased among women with a family history of breast cancer and current and past users of menopausal hormone therapy (MHT).

The Women’s Health Initiative study, which documented the association between MHT use and invasive breast cancer, also reported on associations between MHT use and DCIS.70 The results for DCIS, while not statistically significant, were in the same direction as the results for invasive breast cancer, suggesting that estrogen plus progestin use may be associated with an increased risk of DCIS, while estrogen-alone use may be associated with a decreased risk.70 An important feature of the study was that all participants had regular screening mammography, which ensured that hormone users and nonhormone users had an equal probability of DCIS detection.

Clinical trials of chemoprevention agents for women at high risk of breast cancer have found decreased incidence of DCIS among women receiving tamoxifen or raloxifene.71 A clinical trial of exemestane for breast cancer prevention demonstrated a significant reduction in the incidence of invasive cancer and in the incidence of invasive cancer and DCIS combined; however, the incidence of DCIS was not significantly decreased (HR, 0.65; 95% CI, 0.28–1.51).72 In a more recent clinical trial, anastrozole significantly decreased the incidence of DCIS (HR, 0.30; 95% CI, 0.32–0.68).73

Cancer Statistics: Breast Cancer in Situ
Selected Findings

Breast Carcinoma In Situ Incidence 2007-2011

Diagnosis of in situ breast cancer rarely occurs among women younger than 40 years, the age at which the American Cancer Society and some other organizations have recommended that women of average risk for breast cancer begin mammography screening. DCIS incidence rates increase with age and peak at ages 70 to 79 years, whereas LCIS incidence rates peak at ages 50 to 59 years (Fig. 1). The age-specific incidence of IDC parallels the age-specific incidence of DCIS, while the peak in ILC occurs at age 65 years and older (Fig. 1). Age-specific rates for invasive breast cancers of all other histologic types combined show a continuing rise with age (Fig. 1).

TABLE 2. Breast Carcinoma In Situ Incidence Rates by Race, Ethnicity and Age, 2007 to 2011*

| AGE, YEARS | ALL RACES | NON-HISPANIC WHITE | NON-HISPANIC BLACK | ASIAN AND PACIFIC ISLANDER | AMERICAN INDIAN AND ALASKA NATIVE† | HISPANIC |
|------------|-----------|---------------------|---------------------|-----------------------------|-----------------------------------|---------|
| DCIS       | All ages  | 25.8                | 26.6                | 26.5                        | 23.9                              | 14.4    | 17.9   |
|            | 20-39     | 3.4                 | 3.7                 | 3.5                         | 3.4                               | 1.9     | 2.1    |
|            | 40-49     | 37.9                | 40.7                | 32.8                        | 42.1                              | 20.5    | 25.9   |
|            | 50-59     | 57.9                | 59.8                | 56.9                        | 57.0                              | 33.4    | 41.7   |
|            | 60-69     | 81.8                | 82.9                | 91.3                        | 70.1                              | 49.6    | 58.2   |
|            | 70-79     | 84.3                | 85.8                | 94.6                        | 66.8                              | 46.3    | 57.2   |
|            | ≥80       | 47.4                | 47.6                | 55.8                        | 33.2                              | 19.4    | 32.2   |
| LCIS       | All ages  | 3.9                 | 4.4                 | 2.6                         | 2.1                               | —       | 2.7    |
|            | 20-39     | 0.6                 | 0.7                 | 0.4                         | 0.5                               | —       | 0.4    |
|            | 40-49     | 9.4                 | 10.8                | 5.5                         | 6.0                               | —       | 6.6    |
|            | 50-59     | 11.2                | 12.7                | 7.2                         | 5.5                               | —       | 7.4    |
|            | 60-69     | 8.6                 | 9.3                 | 6.4                         | 3.5                               | —       | 6.3    |
|            | 70-79     | 6.0                 | 6.5                 | 5.1                         | 2.2                               | —       | 3.6    |
|            | ≥80       | 2.4                 | 2.6                 | 2.0                         | 1.3                               | —       | 1.5    |

DCIS indicates ductal carcinoma in situ; LCIS, lobular carcinoma in situ.

*Rates are per 100,000 population and age adjusted to the 2000 US standard population.

†Data based on Indian Health Service Contract Health Service Delivery Areas. Rates for LCIS not shown because of sparse data.

Source: North American Association of Central Cancer Registries, 2014.
Overall DCIS incidence rates are nearly identical for NH white and NH black women, somewhat lower for Asian/Pacific Islander women; lower among Hispanic women; and lowest for American Indian/Alaska Native women (Table 2). LCIS incidence rates are almost twice as high among NH white women compared with other population groups (Table 2). Lower incidence rates in Hispanic and American Indian/Alaska Native women may be caused in part by inaccurate identification of race and ethnicity in cancer registries as well as lower access to and utilization of mammographic screening.

Table 3 shows the distribution of prognostic factors among DCIS lesions diagnosed during 2007 through 2011. The majority of lesions are small (≤1.5 cm) (47%), grade II (34%) or III (36%), and histologic type “DCIS, not otherwise specified (NOS)” (68%). Similar to invasive breast cancer, most DCIS lesions are ER-positive (72% vs 74% of invasive breast cancers). The distribution of ER

### Table 3. Distribution of Prognostic Characteristics Among Ductal Carcinoma In Situ Cases by Race and Ethnicity, 2007 to 2011

| PROGNOSTIC CHARACTERISTIC | ALL RACES | NON-HISPANIC WHITE | NON-HISPANIC BLACK | ASIAN AND PACIFIC ISLANDER | AMERICAN INDIAN AND ALASKA NATIVE* | HISPANIC |
|---------------------------|-----------|---------------------|--------------------|----------------------------|-----------------------------------|----------|
| Hormone receptor status†  |           |                     |                    |                            |                                   |          |
| ER +                       | 72%       | 71%                 | 75%                | 75%                        | 66%                               | 70%      |
| ER −                       | 13%       | 13%                 | 11%                | 12%                        | 14%                               | 11%      |
| Missing                    | 16%       | 15%                 | 15%                | 14%                        | 20%                               | 19%      |
| Tumor grade                |           |                     |                    |                            |                                   |          |
| Grade I                    | 14%       | 14%                 | 15%                | 13%                        | 16%                               | 14%      |
| Grade II                   | 34%       | 33%                 | 36%                | 40%                        | 31%                               | 34%      |
| Grade III                  | 36%       | 37%                 | 31%                | 36%                        | 34%                               | 34%      |
| Missing                    | 16%       | 16%                 | 18%                | 12%                        | 19%                               | 18%      |
| Histologic subtype§        |           |                     |                    |                            |                                   |          |
| DCIS, NOS                  | 68%       | 68%                 | 68%                | 68%                        | 66%                               | 69%      |
| Comedocarcinoma            | 10%       | 10%                 | 9%                 | 9%                         | 13%                               | 9%       |
| Papillary                  | 2%        | 2%                  | 3%                 | 2%                         | 2%                                | 2%       |
| Micropapillary             | 2%        | 2%                  | 3%                 | 2%                         | 2%                                | 2%       |
| Cribriform                 | 10%       | 10%                 | 10%                | 11%                        | 10%                               | 10%      |
| Solid                      | 8%        | 8%                  | 7%                 | 7%                         | 7%                                | 7%       |
| Tumor size, cm             |           |                     |                    |                            |                                   |          |
| ≤1.5                       | 47%       | 48%                 | 43%                | 49%                        | 50%                               | 45%      |
| 1.6-4.0                    | 15%       | 15%                 | 16%                | 21%                        | 14%                               | 16%      |
| >4.0                       | 5%        | 5%                  | 7%                 | 6%                         | 5%                                | 5%       |
| Missing                    | 33%       | 33%                 | 34%                | 24%                        | 31%                               | 34%      |

*Data are based on Indian Health Service Contract Health Service Delivery Areas.
†Hormone receptor status is based on cases diagnosed between 2009 and 2011 with more complete data.
‡ER-positive includes borderline findings.
§Cancer registries report information regarding architectural patterns of DCIS under the heading of histologic subtype.
Percentages may not sum to 100 because of rounding.
Source: North American Association of Central Cancer Registries, 2014.

Overall DCIS incidence rates are nearly identical for NH white and NH black women, somewhat lower for Asian/Pacific Islander black women, lower among Hispanic women; and lowest for American Indian/Alaska Native women (Table 2). LCIS incidence rates are almost twice as high among NH white women compared with other population groups (Table 2). Lower incidence rates in Hispanic and American Indian/Alaska Native women may be caused in part by inaccurate identification of race and ethnicity in cancer registries as well as lower access to and utilization of mammographic screening.

Table 4 shows the distribution of prognostic factors among DCIS lesions diagnosed during 2007 through 2011. The majority of lesions are small (≤1.5 cm) (47%), grade II (34%) or III (36%), and histologic type “DCIS, not otherwise specified (NOS)” (68%). Similar to invasive breast cancer, most DCIS lesions are ER-positive (72% vs 74% of invasive breast cancers). The distribution of ER

### Table 4. Incidence Trends for Ductal Carcinoma In Situ and Lobular Carcinoma In Situ by Age, 1992 to 2011

| AGE, YEARS | TREND 1 | TREND 2 | TREND 3 |
|------------|---------|---------|---------|
| DCIS       |         |         |         |
| >20        | 1992-1999 | 7.9*   | 1999-2011 | 0.8*  |
| 40-49      | 1992-1998 | 7.3*   | 1998-2011 | 2.0*  |
| 50-69      | 1992-1999 | 8.8*   | 1999-2011 | 0.4   |
| 70-79      | 1992-1998 | 9.5*   | 1998-2011 | 1.1*  |
| LCIS       |         |         |         |
| >20        | 1992-2011 | 1.2*   |         |       |
| 40-49      | 1992-2011 | 1.7*   |         |       |
| 50-69      | 1992-2001 | 4.4*   | 2001-2004 | −7.2  |
| 70-79      | 1992-2011 | 1.4*   | 2004-2011 | 2.1   |

APC indicates annual percent change; DCIS, ductal carcinoma in situ; LCIS, lobular carcinoma in situ.
*This trend is significantly different from zero (P < .05.) Incidence trends were adjusted for reporting delay.
Source: Surveillance, Epidemiology, and End Results (SEER) Program, 13 SEER registries.
status does not differ markedly by race, unlike invasive breast cancer, for which NH black women have a notably higher percentage of ER-negative tumors than women of other races/ethnicities (28% vs 15%-19%, respectively). There is little variability in grade, histologic subtype, and tumor size by race/ethnicity; NH black women are slightly less likely to have high-grade tumors and more likely to have large tumors than other groups.

**Breast Carcinoma In Situ Incidence Trends**

The incidence of in situ breast cancers increased rapidly after the introduction of mammography as a population screening tool in the United States from the late 1980s until about 1998, and subsequently increased at a slower rate. Joinpoint analyses of DCIS incidence trends for women aged 20 years and older found an annual percent change (APC) of 7.9% from 1992 to 1999 and an APC of 0.8% from 1999 to 2011 (Table 4). For LCIS, Joinpoint analyses found an increasing trend of 1.2% per year from 1992 to 2011 (Table 4). The reasons why the incidence of DCIS and LCIS continued to increase after mammography rates plateaued around the year 2000 are not known. However, possible explanations include the widespread transition from screen-film to digital mammography, which may have increased the rate of detection of these lesions. Analyses of data collected in the Breast Cancer Screening Consortium (BCSC) did not find an increasing trend in the frequency of biopsies after screening mammograms from 1996 to 2008 but did find mild increases in the frequency of invasive cancer and DCIS detected in these biopsies among women ages 40 to 69 years.

Incidence rates from 1992 to 2011 for DCIS and LCIS are shown for 3 age groups of women in Figure 2 and are described in Table 4. Incidence rates for DCIS among women in all 3 age groups rose rapidly during the 1990s, then plateaued for women ages 50 to 69 years from 1999 to 2011, but continued to increase at a slower rate for women ages 40 to 49 years and 70 to 79 years from 1998 to 2011. Incidence rates for LCIS, in contrast, significantly increased at a modest rate for women ages 40 to 49 years and 70 to 79 years from 1992 to 2011; while, for women ages 50 to 69 years, rates increased rapidly from 1992 to 2001, showed a nonsignificant decline of 7.2% per year from 2001 to 2004, then levelled-off from 2004 to 2011. The change in trend among women ages 50 to 69 years during 2001 through 2004 likely results from declines in the use of combined MHT after the Women’s Health Initiative study reported an increased risk of invasive breast cancer.

**FIGURE 2. Trends in Ductal Carcinoma In Situ and Lobular Carcinoma In Situ Incidence Rates by Age at Diagnosis, 1992 to 2011.**

Rates are age adjusted to the 2000 US standard population and adjusted for delays in reporting. Dots indicate observed rates and solid lines indicate modeled rates. Source: Surveillance, Epidemiology, and End Results (SEER) Program, 13 SEER registries.
Previous studies have demonstrated declines in invasive breast cancer incidence in the early 2000s. A study of women enrolled in the BCSC reported a significant decline in DCIS incidence among women ages 50 to 79 years from 2002 to 2006. The BCSC study also found that MHT use among women ages 50 to 69 years declined from a steady state of 4800 per 10,000 screening mammograms from 1997 to 2001 to approximately 1300 per 10,000 screening mammograms in 2006. The decline in LCIS incidence among women ages 50 to 69 years is notable, because studies have shown stronger associations between MHT use and ILC than between MHT use and IDC.

Treatment Patterns for DCIS and LCIS

Figure 3 illustrates surgical treatment patterns for women who were diagnosed with a first primary DCIS or LCIS in the United States from 2007 to 2011. Among women of all ages who were treated for DCIS, BCS was the most common surgical treatment (69%), followed by unilateral mastectomy (19%), bilateral mastectomy (8%), and no surgery (4%). Age at diagnosis was strongly associated with surgical treatment received, with younger women substantially more likely to receive bilateral mastectomy (Fig. 3). In fact, the majority of DCIS patients younger than 40 years underwent mastectomy (53%), opting for bilateral mastectomy slightly more often than unilateral mastectomy (28% vs 25%, respectively). Although NCCN treatment guidelines for DCIS do not formally stratify surgical recommendations by age, it is one of the factors considered in the University of Southern California/Van Nuys Prognostic Index, which is used to predict local recurrences for women with DCIS. Clinical trials and population studies of DCIS outcomes generally find higher recurrence rates for younger women (younger than 50 years) compared with older women. In addition, younger women have a longer life expectancy and, thus, a greater cumulative probability of experiencing a second breast event and/or multiple diagnostic mammograms and biopsies in the course of posttreatment surveillance, which may influence preferences for mastectomy over BCS for younger women.

Surgical treatment for LCIS most often involved BCS (80% of women of all ages), followed by no surgical treatment (11%), bilateral mastectomy (5%), and unilateral mastectomy (4%). It should be noted that BCS for LCIS more commonly involves a smaller segment of the breast than BCS for DCIS, as the primary purpose is diagnostic rather than therapeutic. Mastectomy was slightly more common among younger women, with 9% of LCIS patients aged 40 years and younger undergoing bilateral mastectomy and 4% undergoing unilateral mastectomy.

Further analyses were conducted of the sociodemographic and clinical characteristics associated with treatment for DCIS, with treatment types categorized as BCS plus RT (BCS + RT), BCS without radiation (BCS no RT), unilateral mastectomy, and bilateral mastectomy. These analyses confirmed that age remained an important
predictor of treatment after controlling for clinical and demographic characteristics (Table 5). Multinomial analyses with BCS + RT as the referent treatment and ages 50 to 59 years as the referent age group confirmed the descriptive finding of a higher odds of unilateral and bilateral mastectomy for young women but also found a modestly increased odds of BCS without RT versus BCS + RT among women aged 40 years and younger. In addition, older age was associated with higher odds of BCS without RT and unilateral mastectomy and with lower odds of bilateral mastectomy. Analyses of treatment variations by race/ethnicity, with NH white women as the referent group, confirmed relatively modest variations in treatment patterns, with “NH other” (primarily Asian) women having lower odds of receiving BCS without RT, and Hispanic, NH black, and NH other women having modestly higher odds of undergoing unilateral mastectomy and substantially lower odds of undergoing bilateral mastectomy (Table 5).

Treatment patterns for DCIS were fairly stable during the time period from 2007 to 2011, although the percentage of women treated with bilateral mastectomy increased from 7.1% in 2007 (referent) to 9.5% in 2011 (trend

### Table 5. Patterns and Predictors of Treatment for Ductal Carcinoma In Situ, 2007 to 2011

|                      | BCS + RT, N = 44,182 | BCS + NO RT, N = 18,008 | UNILATERAL, N = 17,629 | BILATERAL, N=7,422 |
|----------------------|----------------------|-------------------------|------------------------|--------------------|
| **Age, years**       |                      |                         |                        |                    |
| 20-39                | 776                  | 28.5                    | 351                    | 12.9              |
| 40-49                | 8,918                | 48.5                    | 2,749                  | 14.9              |
| 50-59                | 13,651               | 54.7                    | 4,350                  | 17.4              |
| 60-69                | 12,649               | 55.9                    | 4,557                  | 20.1              |
| 70-79                | 6,627                | 49.1                    | 3,687                  | 27.3              |
| >80                  | 1,961                | 30.9                    | 2,314                  | 45.9              |
| **Race/ethnicity**   |                      |                         |                        |                    |
| NH white             | 33,579               | 51.2                    | 13,429                 | 20.5              |
| Hispanic             | 2,874                | 48.7                    | 1,357                  | 23.0              |
| NH black             | 4,837                | 50.2                    | 1,968                  | 20.4              |
| NH other             | 2,620                | 48.4                    | 1,040                  | 19.2              |
| Unknown              | 272                  | 37.9                    | 214                    | 37.9              |
| **Year of diagnosis**|                      |                         |                        |                    |
| 2007                 | 8,040                | 51.9                    | 3,245                  | 21.0              |
| 2008                 | 8,437                | 51.3                    | 3,398                  | 20.7              |
| 2009                 | 9,108                | 50.2                    | 3,853                  | 21.2              |
| 2010                 | 8,916                | 50.4                    | 3,524                  | 20.1              |
| 2011                 | 9,681                | 50.4                    | 3,988                  | 20.7              |
| **Tumor size, cm**   |                      |                         |                        |                    |
| ≤1.5                 | 33,247               | 55.3                    | 14,173                 | 23.6              |
| 1.6-4.0              | 9,241                | 45.2                    | 3,116                  | 15.2              |
| >4.0                 | 1,694                | 25.5                    | 719                    | 10.8              |
| **Histology subgroup**|                      |                         |                        |                    |
| DCIS, NOS            | 29,115               | 50.2                    | 11,757                 | 20.3              |
| Comedo              | 4,847                | 53.0                    | 1,270                  | 13.9              |
| Other                | 10,220               | 50.4                    | 4,981                  | 24.8              |
| Unknown              | 5,250                | 53.1                    | 2,104                  | 21.3              |
| **Tumor grade**      |                      |                         |                        |                    |
| Grade I              | 6,610                | 50.2                    | 6,610                  | 20.3              |
| Grade II             | 18,088               | 51.2                    | 8,023                  | 22.7              |
| Grade III            | 19,484               | 50.9                    | 5,568                  | 14.5              |
| **Census region**    |                      |                         |                        |                    |
| Northeast            | 8,097                | 54.3                    | 3,053                  | 20.5              |
| Midwest              | 11,703               | 57.4                    | 3,216                  | 15.8              |
| South               | 12,723               | 48.7                    | 5,209                  | 20.0              |
| West                | 11,659               | 45.2                    | 6,530                  | 25.3              |

BCS indicates breast-conserving surgery; DCIS, ductal carcinoma in situ; LCIS, lobular carcinoma in situ; NH, non-Hispanic; NO RT, no radiotherapy; OR, odds ratio; Ref, reference group; RT, radiotherapy.

*The OR is significantly different from 1.00 (P < .05).

Source: North American Association of Central Cancer Registries, 2014. 5
treatment than for other forms of therapy, so the actual evidence for several molecular biological markers associated with DCIS and candidate markers associated with increased risk of ipsilateral recurrence after DCIS treatment. None of the biologic markers, which included steroid receptors, proliferation markers, cell–cycle regulation and apoptotic markers, angiogenesis-related proteins, epidermal growth factor family receptors, extracellular matrix-related proteins, and cyclooxygenase-2, were consistently associated with the risk of local recurrence. Most of the studies included in the review were limited to small patient cohorts in which treatment varied from patient to patient and methods for determining biomarker expression were variable.

One proposed explanation for the limited progress in identifying molecular changes in DCIS cells that are associated with the risk of subsequent invasion is that the pathophysiology of invasion involves interplay between the DCIS cells and the adjacent myoepithelial cells. The best known function of these contractile cells is in the ejection of milk from the lactating breast, but experimental evidence also suggests an important role in suppressing mammary carcinogenesis and progression and indicates that molecular changes in paracrine communication between myoepithelial cells and epithelial cells of DCIS lesions may represent prognostic markers and therapeutic targets. Likewise, emerging research suggests pathophysiologic and potential therapeutic importance of the paracrine interactions between DCIS epithelial cells and a variety of mammary stromal components, such as extracellular matrix components, inflammatory/immune system cells, and fibroblasts.

A recent study of molecular markers in patients with concurrent DCIS and IDC found considerable intraindividual heterogeneity in DCIS lesions in individual patients for progesterone receptor, HER2, Ki67, and p16 expression, further highlighting the complexity of studying the clinical relevance of prognostic markers for these precursor lesions. That study identified a subtype of DCIS with immunohistochemical characteristics similar to those of invasive breast cancers in the same patients (high Ki67 expression, increased nuclear accumulation of mutant p53, and low p16 expression) and suggested that these DCIS lesions might be particularly likely to progress to invasion.

There has also been recent interest in evaluating molecular subtypes of DCIS in relation to prognosis. Because targeted anti–HER2 therapies are not standard treatment for DCIS, HER2 testing is not a routine part of the pathologic evaluation. However, studies suggest that high-nuclear-grade DCIS lesions are often negative for ER and overexpress HER2. Targeting HER2 is a potential treatment strategy for HER2-overexpressing DCIS and addresses the lack of targeted therapy in this subgroup of patients, many of whom lack ER and will not benefit from tamoxifen. Given experimental evidence that
trastuzumab enhances radiosensitivity of HER2-expressing cancer cells and the acceptable safety profile, a current clinical trial is comparing treatment with whole-breast irradiation alone versus 2 intravenous administrations of trastuzumab given concurrently with whole-breast irradiation for women with HER2-positive DCIS (National Surgical Adjuvant Breast and Bowel Project–43). A multigene expression assay (the DCIS Score) has recently been developed to predict the probability of local recurrence of DCIS or invasive carcinoma after surgical excision without radiation. The DCIS Score includes 7 cancer-related genes and 5 reference genes and is interpreted on a scale from 0 to 100, with risk categories of low (scores <39), intermediate (scores of 39-54), and high (scores ≥55). This score has been evaluated as a predictor of recurrence in a prospective multicenter trial designed to evaluate treatment using surgical excision without radiation for women who had either low-grade or intermediate-grade DCIS with tumor size ≤2.5 cm or high-grade DCIS with tumor size <1.0 cm. The study demonstrated that women with a low DCIS Score were significantly less likely to have any breast event or an invasive breast event during the 10 years of follow-up than those with an intermediate or high score. A separate population-based study in Ontario was conducted to test the DCIS Score as a predictor of recurrence risk in patients treated with BCS alone and in patients treated with BCS + RT, all of whom had clear margins. The study found that the DCIS Score predicted the 10-year rate of ipsilateral breast recurrence in both treatment groups. Among patients treated with BCS alone, recurrence rates by DCIS Score risk group were: low, 12.7%; intermediate, 33.0%; and high, 27.8% (P < .001). Among women treated with BCS + RT, recurrence rates by DCIS Score risk group were: low, 7.5%; intermediate, 13.6%; and high, 20.5% (P < .001).

Conclusions

Despite progress in understanding the molecular and clinical heterogeneity of in situ breast cancers and efforts to better target treatments based on the likelihood of progression or recurrence, there remain many uncertainties for women with these conditions. Lack of understanding of their diagnosis and its implications may result in unnecessary psychological burden for women with in situ breast cancers. There is an important role of patient and provider communication and informed decision making in mitigating these risks. As molecular and clinical research continues to seek clearer answers and better therapies, there is a concurrent need for the development of more effective patient communication tools for in situ cancers, focusing on the nature of the disease, treatment options, and prognosis.

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