



Breast Cancer

Facts & Figures 2017-2018



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Breast Cancer Basic Facts

What is breast cancer?

Cancer is a group of diseases that cause cells in the body to change and spread out of control. Most types of cancer cells eventually form a lump or mass called a tumor, and are named after the part of the body where the tumor originates. Most breast cancers begin either in the breast tissue made up of glands for milk production, called lobules, or in the ducts that connect the lobules to the nipple. The remainder of the breast is made up of fatty, connective, and lymphatic tissues.

What are the signs and symptoms of breast cancer?

Breast cancer typically produces no symptoms when the tumor is small and most easily treated, which is why screening is important for early detection. The most common physical sign is a painless lump. Sometimes breast cancer spreads to underarm lymph nodes and causes a lump or swelling, even before the original breast tumor is large enough to be felt. Less common signs and symptoms include breast pain or heaviness; persistent changes, such as swelling, thickening, or redness of the skin; and nipple abnormalities such as spontaneous discharge (especially if bloody), erosion, or retraction. Any persistent change in the breast should be evaluated by a physician as soon as possible.

Table 1. Estimated New Female Breast Cancer Cases and Deaths by Age, US, 2017

Age	In Situ Cases		Invasive Cases		Deaths	
	Number	%	Number	%	Number	%
<40	1,610	3%	11,160	4%	990	2%
40-49	12,440	20%	36,920	15%	3,480	9%
50-59	17,680	28%	58,620	23%	7,590	19%
60-69	17,550	28%	68,070	27%	9,420	23%
70-79	10,370	16%	47,860	19%	8,220	20%
80+	3,760	6%	30,080	12%	10,910	27%
All ages	63,410		252,710		40,610	

Estimates are rounded to the nearest 10. Percentages may not sum to 100 due to rounding.

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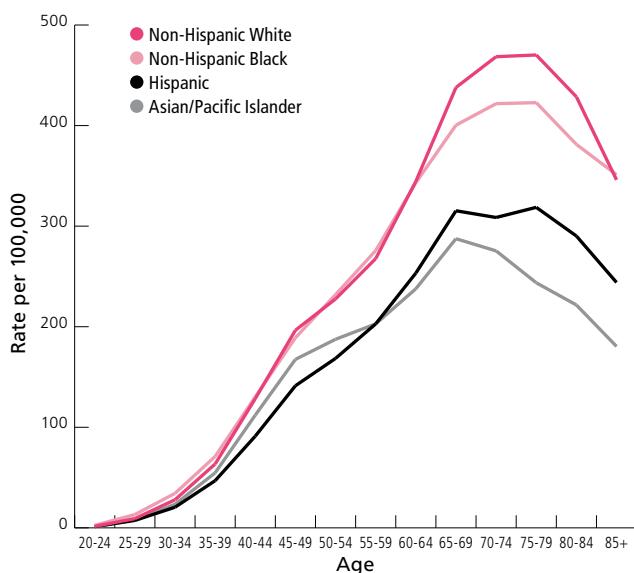
How is breast cancer diagnosed?

Breast cancer is typically detected either during a screening examination, before symptoms have developed, or after a woman notices a lump. Most masses seen on a mammogram and most breast lumps turn out to be benign (not cancerous), do not grow uncontrollably or spread, and are not life-threatening. When cancer is suspected, microscopic analysis of breast tissue is necessary for a diagnosis and to determine the extent of spread (stage) and characterize the type of the disease. The tissue for microscopic analysis can be obtained from a needle biopsy (fine-needle or wider core needle) or surgical incision. Selection of the type of biopsy is based on multiple factors, including the size and location of the mass, as well as patient factors and preferences and resources.

How is breast cancer staged?

The prognosis of invasive breast cancer is strongly influenced by the stage of the disease – that is, the extent or spread of the cancer when it is first diagnosed. There are two main staging systems for cancer. The TNM classification of tumors uses information on tumor size and how far it has spread within the breast and to adjacent tissues (T), the extent of spread to the nearby lymph nodes (N), and the presence or absence of distant metastases (spread to distant organs) (M).¹ Once the T, N, and M are determined, a stage of 0, I, II, III, or IV is assigned, with stage 0 being *in situ* (abnormal cells have not penetrated the ducts or glands from which they originated), stage I being early-stage invasive cancer, and stage IV being the most advanced disease. The TNM staging system is commonly used in clinical settings. The latest revision (8th edition) to the TNM stage for breast cancer also incorporates biologic factors in order to further refine the breast cancer staging system and will be implemented by oncology programs in 2018.²

Figure 1. Age-specific Female Breast Cancer Incidence Rates by Race/Ethnicity, 2010-2014, US



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

Sources: Incidence: North American Association of Central Cancer Registries (NAACCR), 2017. Mortality: National Center for Health Statistics, Centers for Disease Control and Prevention, 2017.

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The Surveillance, Epidemiology, and End Results (SEER) Summary Stage system is more simplified and is commonly used in reporting cancer registry data and for public health research and planning.

According to the SEER Summary Stage system:

- In situ stage refers to the presence of abnormal cells that have not invaded nearby tissues (corresponding to stage 0 in the TNM staging system).
- Local stage refers to cancers that are confined to the breast (corresponding to stage I and some stage II cancers).
- Regional stage refers to tumors that have spread to surrounding tissue or nearby lymph nodes (generally corresponding to stage II or III cancers, depending on size and lymph node involvement).
- Distant stage refers to cancers that have metastasized (spread) to distant organs or lymph nodes above the collarbone (corresponding to some stage IIIc and all stage IV cancers).

What are the types of breast cancer?

In Situ

There are two main types of in situ breast cancer: ductal carcinoma in situ (DCIS) and lobular carcinoma in situ (LCIS), also known as lobular neoplasia. Other in situ breast cancers have characteristics of both ductal and lobular carcinomas or have unknown origins.

- **Ductal carcinoma in situ.** DCIS (83% of in situ cases diagnosed during 2010-2014) refers to a condition in which abnormal cells replace the normal epithelial cells that line the breast ducts and may greatly expand the ducts and lobules. DCIS may or may not progress to invasive cancer; in fact, sometimes DCIS grows so slowly that even without treatment it would not affect a woman's health. Long-term studies of women whose DCIS was untreated because it was originally misclassified as benign found that 20%-53% were diagnosed with an invasive breast cancer over the course of 10 or more years.³⁻⁷
- **Lobular carcinoma in situ.** LCIS (13% of in situ cases) refers to abnormal cells growing within and expanding some of the lobules of the breast. LCIS is generally not thought to be a precursor of invasive cancer, but is a strong risk factor for developing invasive cancer.

See pages 13 and 24 for additional information on DCIS and LCIS. More information can also be found in the *Cancer Facts & Figures 2015*, Special Section: Breast Carcinoma In Situ.

Invasive

Most (80%) breast cancers are invasive, or infiltrating, which means they have broken through the walls of the glands or ducts where they originated and grown into surrounding breast tissue. Although breast cancer generally has been referred to as a single disease, there are up to 21 distinct histological subtypes and at least four different molecular subtypes that differ in terms of risk factors, presentation, response to treatment, and outcomes.⁸⁻¹⁰ Gene expression profiling techniques have allowed better understanding of the molecular subtypes of breast cancers; however, this is a costly and complicated

process and is not currently standard practice. Approximations of molecular subtypes have been identified using routinely evaluated biological markers, including the presence or absence of hormone (estrogen or progesterone) receptors (HR+/HR-) and excess levels of human epidermal growth factor receptor 2 (HER2, a growth-promoting protein) and/or extra copies of the *HER2* gene (HER2+/HER2-).¹¹ The four main molecular subtypes and their distribution are described here.

- **Luminal A (HR+/HER2-)** (71%). These cancers tend to be slow-growing and less aggressive than other subtypes. Luminal A tumors are associated with the most favorable prognosis, particularly in the short term, in part because they are more responsive to anti-hormone therapy (see page 27).^{12, 13}
- **Triple negative (HR-/HER2-)** (12%). So called because they are estrogen receptor (ER)-, progesterone receptor (PR)-, and HER2-, these cancers are twice as common in black women as white women in the US, and are also more common in premenopausal women and those with a *BRCA1*

gene mutation.¹⁴ The majority (about 75%) of triple negative breast cancers fall in to the basal-like subtype defined by gene expression profiling. Triple negative breast cancers have a poorer short-term prognosis than other subtypes, in part because there are currently no targeted therapies for these tumors.¹⁵

- **Luminal B (HR+/HER2+)** (12%). Like luminal A cancers, luminal B cancers are ER+ and/or PR+ and are further defined by being highly positive for Ki67 (indicator of a large proportion of actively dividing cells) or HER2. Luminal B breast cancers tend to be higher grade and are associated with poorer survival than luminal A cancers.¹³
- **HER2-enriched (HR-/HER2+)** (5%). HER2-enriched cancers tend to grow and spread more aggressively than other subtypes and are associated with poorer short-term prognosis compared to HR+ breast cancers.¹³ However, the recent widespread use of targeted therapies for HER2+ cancers has improved outcomes for these patients. For more information about the treatment of HER2+ breast cancers, see the section on targeted therapy on page 28.

Breast Cancer Occurrence

How many cases and deaths are estimated to occur in 2017?

In 2017, an estimated 252,710 new cases of invasive breast cancer will be diagnosed among women (Table 1, page 1) and 2,470 cases will be diagnosed in men. In addition, 63,410 cases of in situ breast carcinoma will be diagnosed among women. Approximately 40,610 women and 460 men are expected to die from breast cancer in 2017.

How many women alive today have ever had breast cancer?

More than 3.5 million US women with a history of breast cancer were alive on January 1, 2016.¹⁶ Some of these women were cancer-free, while others still had evidence of cancer and may have been undergoing treatment.

Who gets breast cancer?

Age

- Breast cancer incidence and death rates generally increase with age (Figure 1). The decrease in incidence rates that occurs in women 80 years of age and older may reflect lower rates of screening, the detection of cancers by mammography before 80 years of age, and/or incomplete detection.
- During 2010-2014, the median age at the time of breast cancer diagnosis was 62.¹⁷ This means that half of women who developed breast cancer were 62 years of age or younger at the time of diagnosis. The median age of diagnosis is younger for black women (59) than white women (63).¹⁷

Table 2. Age-specific Probability of Developing Invasive Breast Cancer for US Women

Current age	10-year probability:	or 1 in:
20	0.1%	1,567
30	0.5%	220
40	1.5%	68
50	2.3%	43
60	3.4%	29
70	3.9%	25
Lifetime risk	12.4%	8

Note: Probability is among those free of cancer at beginning of age interval. Based on cases diagnosed 2012-2014. Percentages and "1 in" numbers may not be numerically equivalent due to rounding.

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- A woman living in the US has a 12.4%, or a 1-in-8, lifetime risk of being diagnosed with breast cancer (Table 2). Conversely, 7 out of 8 women born today will not be diagnosed with breast cancer in their lifetimes. In the 1970s, the lifetime risk of being diagnosed with breast cancer was 1 in 11. This increase in risk over the past four decades is due to longer life expectancy, as well as increases in breast cancer incidence due in part to changes in reproductive patterns, menopausal hormone use, the rising prevalence of obesity, and increased detection through screening. Lifetime risk reflects an average woman's risk over an entire lifetime, including the possibility that she may die from another cause before she would have been diagnosed with breast cancer and does not apply only to women who live to a very old age.

Race/Ethnicity

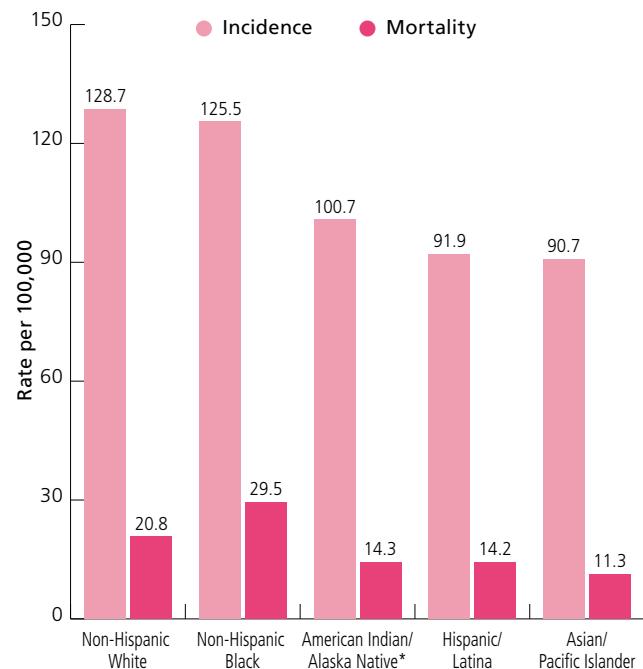
- Figure 2 shows breast cancer incidence and death rates by race and ethnicity during the most recent time period. Incidence and death rates for breast cancer are higher among non-Hispanic white (NHW) and non-Hispanic black (NHB) women than other racial and ethnic groups. Asian/Pacific Islander (API) women have the lowest incidence and death rates.
- Between the ages of 65 and 84, NHW women have markedly higher breast cancer incidence rates than NHB women (Figure 1, page 2). However, NHB women have higher incidence rates before age 40 and are more likely to die from breast cancer at every age.

- Racial/ethnic variation in incidence rates for specific breast cancer subtypes are shown in Figure 3. NHW women have the highest rates of HR+/HER2- breast cancers, whereas NHB women have the highest rates of triple negative breast cancers.

Are there geographic differences in breast cancer rates?

Table 3, page 6 shows the variation in state-level breast cancer incidence and death rates per 100,000 women by race/ethnicity. Although the overall incidence rate for breast cancer in the US remains slightly higher in NHW women compared to NHB women, in 9 of 43 states with data for both groups, rates are higher among NHB women. Data for AI/AN women are too sparse to provide by state; however, a recent study found that rates were more than 2-fold higher among women in Alaska (141.3 per 100,000) than those living in the Southwest US (59.6 per 100,000) during 1999-2009.¹⁸

Figure 2. Female Breast Cancer Incidence (2010-2014) and Mortality (2011-2015) Rates by Race/Ethnicity, US

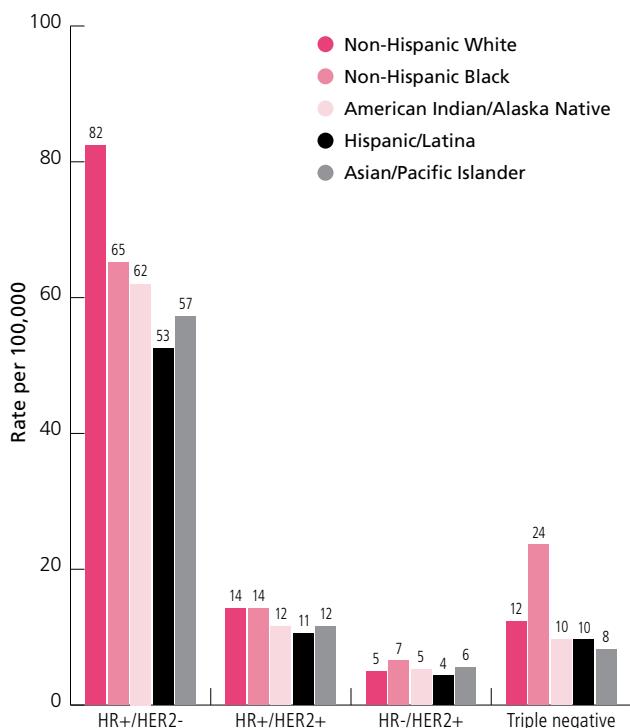


*Statistics based on data from Contract Health Service Delivery Area (CHSDA) counties. Note: Rates are age adjusted to the 2000 US standard population.

Sources: Incidence – NAACCR, 2017. Mortality – National Center for Health Statistics, Centers for Disease Control and Prevention, 2017.

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Figure 3. Female Breast Cancer Incidence Rates by Subtype and Race/Ethnicity, 2010-2014, US



HR = hormone receptor, HER2 = human epidermal growth factor receptor 2.
Note: Rates are age adjusted to the 2000 US standard population.

Source: NAACCR, 2017.

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How has the occurrence of breast cancer changed over time?

Incidence trends

Figure 5, page 8 presents trends for in situ and invasive breast cancer incidence rates since 1975, when population-based cancer registration began in the 9 oldest Surveillance, Epidemiology and End Results (SEER) registries.

Incidence rates of in situ and invasive breast cancer rose rapidly during the 1980s and 1990s (Figure 5a, page 8), largely because of increases in mammography screening. The widespread uptake of mammography screening inflated the incidence rate because cancers were being diagnosed 1 to 3 years earlier than they would have been in the absence of screening, and may also have led to the detection of indolent (very slow-growing) tumors. In addition, some of the historic increase in breast cancer incidence reflects changes in reproductive patterns, such as delayed childbearing and having fewer children, which are known risk factors for breast cancer. The increase in incidence was greater in women 50 years of age and older than in those younger than 50.

Invasive breast cancer rates stabilized between 1987 and 1994 (Figure 5b, page 8). Incidence rates increased again in the latter half of the 1990s, which may reflect further increases in the prevalence of mammography screening, as well as rising rates of obesity and the use of menopausal hormones, both of which increase breast cancer risk. Between 2002 and 2003, invasive breast cancer rates dropped sharply (nearly 7%), likely due to the decreased use of menopausal hormones following the 2002 publication of clinical trial results that found higher risk of breast cancer and heart disease among users.^{19,20} The decline in incidence occurred primarily in white women, in those 50 years of age and older, and for ER+ disease.^{19,21} From 2005 to 2014, the overall invasive breast cancer incidence rate was stable, but the trends vary by race and age.

Incidence rates of in situ breast cancer have been stable since 2000 among women 50 and older and since 2007 among younger women.

Table 3. Female Breast Cancer Incidence (2010-2014) and Mortality (2011-2015) Rates by Race/Ethnicity and State

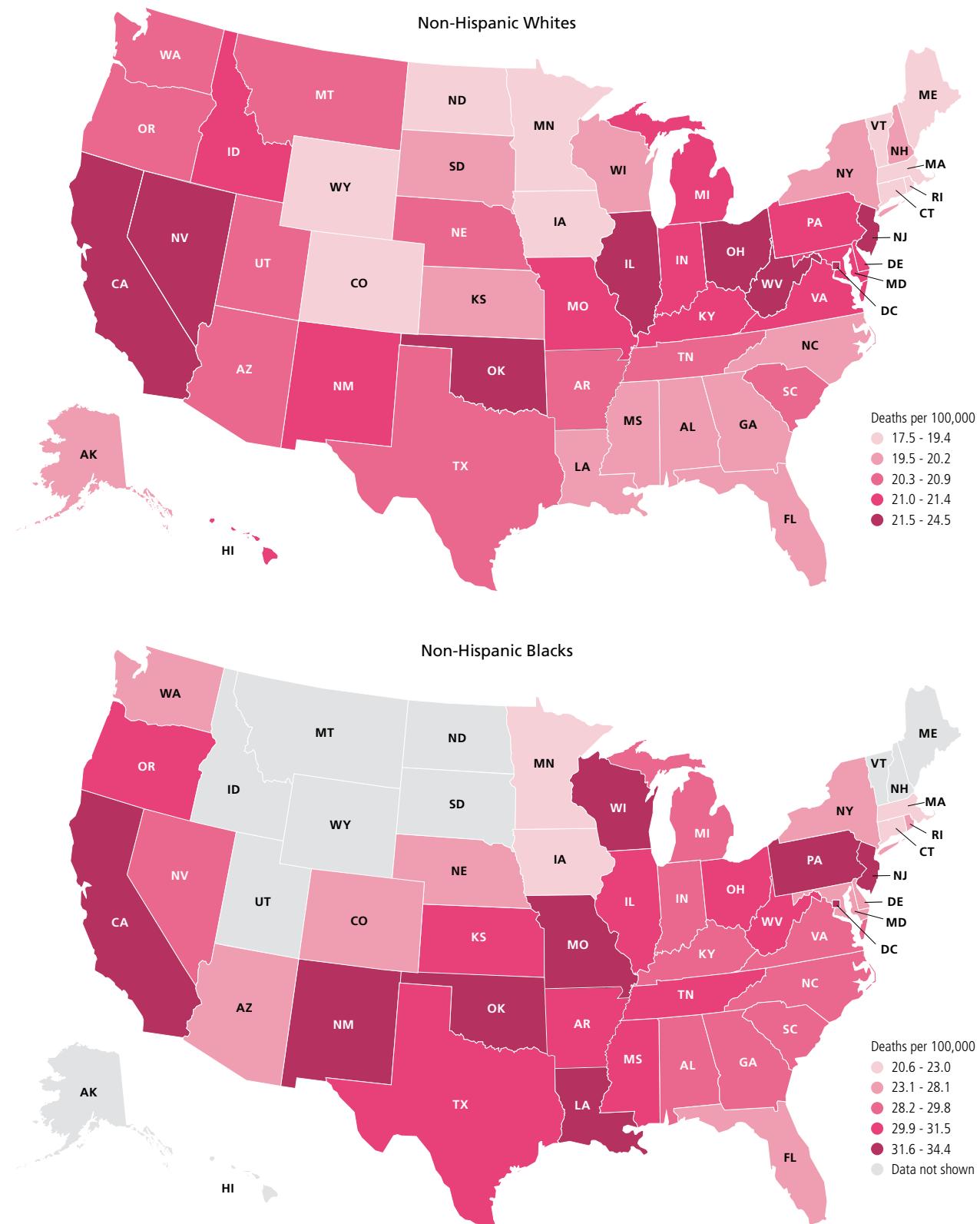
State	Incidence				Mortality			
	Non-Hispanic White	Non-Hispanic Black	Hispanic/Latina	Asian/Pacific Islander	Non-Hispanic White	Non-Hispanic Black	Hispanic/Latina	Asian/Pacific Islander
Alabama	118.2	124.9	64.3	87.4	20.0	28.5	*	*
Alaska	125.9	133.7	80.4	92.3	20.0	*	*	*
Arizona	120.5	107.8	88.9	75.6	20.3	26.2	15.0	12.0
Arkansas	110.5	114.2	148.1	126.9	20.5	30.3	15.3	*
California	139.0	129.0	89.2	95.7	23.1	31.9	14.5	12.6
Colorado	127.1	119.1	104.2	76.1	19.3	25.5	17.2	7.7
Connecticut	143.3	122.9	127.5	89.2	18.9	20.8	10.3	9.0
Delaware	135.8	130.6	100.0	85.9	21.2	26.0	*	*
District of Columbia	157.6	141.6	70.8	90.4	22.6	34.4	*	*
Florida	121.3	108.3	98.1	70.1	20.1	25.8	15.3	9.8
Georgia	125.2	126.3	93.2	74.4	20.1	29.2	10.9	8.8
Hawaii	143.3	120.5	151.6	132.1	21.4	*	*	14.4
Idaho	121.9	*	89.1	76.0	21.3	*	*	*
Illinois	135.7	131.8	89.5	92.7	22.5	31.2	10.9	11.7
Indiana	120.9	130.6	83.7	66.1	21.0	29.6	14.9	*
Iowa	124.7	105.1	67.1	68.2	19.3	21.4	*	*
Kansas	124.4	126.2	84.2	63.2	19.9	30.1	11.6	*
Kentucky	124.3	127.0	54.2	64.4	21.4	28.5	*	*
Louisiana	121.8	132.5	91.5	62.6	20.2	33.6	9.6	*
Maine	126.5	*	*	76.3	18.0	*	*	*
Maryland	135.2	132.4	91.8	84.3	21.2	28.1	10.9	9.2
Massachusetts	141.8	114.7	87.2	87.7	19.1	20.6	10.9	7.2
Michigan	122.0	127.1	80.0	85.3	21.0	29.8	16.2	9.2
Minnesota†	131.5	103.1	103.1	68.9	18.8	23.0	11.4	7.3
Mississippi	113.4	121.0	41.4	60.6	19.5	31.5	*	*
Missouri	126.0	133.4	78.9	88.2	21.3	32.6	10.5	14.4
Montana	122.6	*	134.3	112.5	20.4	*	*	*
Nebraska	123.7	127.8	93.4	65.6	20.3	27.8	*	*
Nevada†	121.3	108.1	75.5	78.5	24.5	29.4	11.2	14.4
New Hampshire	142.3	*	92.2	72.1	20.2	*	*	*
New Jersey	142.3	125.9	98.7	92.2	23.0	32.3	13.2	11.2
New Mexico†	123.2	98.8	103.2	65.6	21.2	32.4	16.8	*
New York	139.6	119.5	101.3	92.2	20.2	26.8	14.7	9.6
North Carolina	130.3	134.1	82.5	77.7	19.7	29.1	10.1	12.1
North Dakota	122.2	*	*	*	17.5	*	*	*
Ohio	123.7	123.8	64.3	79.8	22.2	31.0	9.9	10.9
Oklahoma	114.8	122.9	96.9	80.5	23.0	33.6	13.1	*
Oregon	128.5	127.1	97.0	76.9	20.8	30.0	12.1	9.9
Pennsylvania	131.8	130.8	86.5	73.8	21.2	31.7	12.2	11.2
Rhode Island	135.6	113.4	85.2	68.9	18.8	26.9	*	*
South Carolina	128.8	125.7	89.6	76.3	20.5	29.0	9.4	*
South Dakota	132.1	*	*	*	20.2	*	*	*
Tennessee	121.8	126.3	66.5	70.2	20.7	31.5	11.5	11.6
Texas	122.5	120.3	88.0	65.0	20.6	30.4	15.5	9.9
Utah	116.8	90.3	101.8	91.2	20.9	*	11.8	19.2
Vermont	130.5	*	*	*	19.0	*	*	*
Virginia	130.0	134.3	80.6	79.0	21.0	29.5	11.7	9.8
Washington	139.3	125.7	93.6	98.3	20.9	25.6	9.7	11.1
West Virginia	115.1	120.1	*	77.8	22.2	30.5	*	*
Wisconsin	129.1	133.5	90.2	74.2	19.8	31.6	7.7	*
Wyoming	116.1	*	85.5	*	19.4	*	*	*
United States	128.7	125.5	91.9	90.7	20.8	29.5	14.2	11.3

Note: Rates are per 100,000 and age adjusted to 2000 US standard population. *Statistic not displayed due to fewer than 25 cases or deaths. †This state's registry did not achieve high-quality data standards for one or more years during 2010-2014, according to NAACCR data quality indicators and are not included in the overall US incidence rate.

Sources: Incidence: NAACCR, 2017. Mortality: National Center for Health Statistics, Centers for Disease Control and Prevention, 2017.

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Figure 4. Geographic Variation in Female Breast Cancer Death Rates by Race, 2011-2015

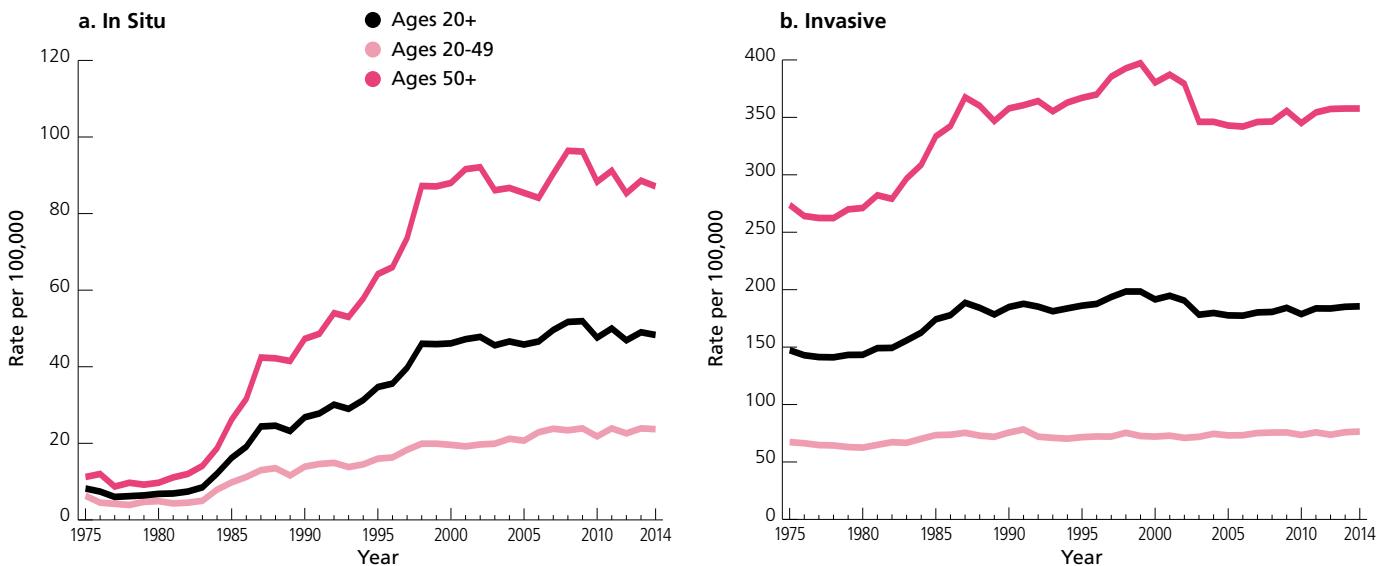


Note: Rates are per 100,000 and age adjusted to the 2000 US standard population. Statistic not displayed for states with fewer than 25 deaths during 2011-2015.

Source: National Center for Health Statistics, Centers for Disease Control and Prevention, 2017.

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Figure 5. Trends in Incidence Rates of Invasive and In Situ Female Breast Cancer by Age, 1975-2014, US



Note: Rates are age adjusted to the 2000 US standard population. Invasive breast cancer rates are adjusted for reporting delay.

Source: Surveillance, Epidemiology, and End Results (SEER) Program, SEER 9 Registries, National Cancer Institute, 2017.

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Race/Ethnicity: Figure 6a presents trends in invasive female breast cancer incidence rates by race and ethnicity. Incidence data are available for white and black women since 1975 and for women of other races and ethnicities since 1992. During 2005-2014, overall breast cancer incidence rates increased among API (1.7% per year), NHB (0.4% per year), and Hispanic (0.3% per year) women, but were stable among NHW and AI/AN women.²²

Age: Trends for invasive breast cancer by age at diagnosis are shown in Figure 5b. Although long-term data (shown) suggest breast cancer incidence rates have increased slightly among women over the age of 50 during the most recent period (2005-2014), data with broader coverage indicate that rates are relatively stable in this age group.²² In contrast, among women under age 50, incidence rates have slowly increased (0.2% per year) since the mid-1990s.²²

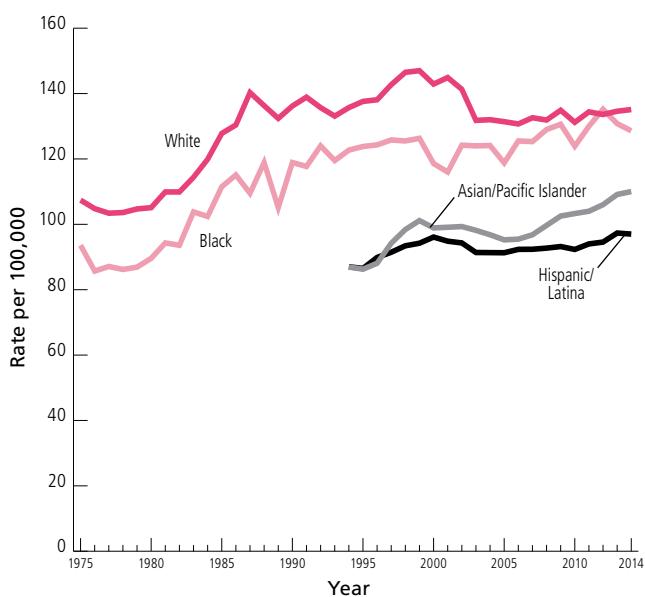
Tumor size: Incidence rates during 2005-2014 were stable for smaller (≤ 2.0 cm) tumors and increased by 1.3% annually for 2.1-5.0 cm tumors and 1.9% annually for tumors larger than 5.0 cm (Figure 7).

Stage: Incidence rates during 2005-2014 increased for localized breast cancer among NHW (0.7% per year), NHB (1.5%), API (2.1%), and Hispanic (0.6%) women; decreased (NHWs, 1.4% per year) or remained stable for regional stage tumors; and increased for distant stage tumors for all groups (NHWs: 2.0% per year; API: 1.7%; Hispanics: 0.7%) except NHBs (Figure 8, page 10).²² Incidence rates for breast cancer with unknown stage decreased in all groups. The decline for regional stage disease in NHWs may reflect a shift toward earlier stage at diagnosis. The increase in distant-stage disease coupled with the decrease in unknown stage may be due to more complete staging of advanced tumors.

Mortality trends

Overall breast cancer death rates increased by 0.4% per year from 1975 to 1989, but have decreased rapidly, for a total decline of 39% through 2015. As a result, 322,600 breast cancer deaths have been averted in US women through 2015. The decrease occurred in both younger and older women, but has slowed among women younger than 50 since 2007. From 2006 through 2015, breast cancer death rates declined annually by 2.6% in

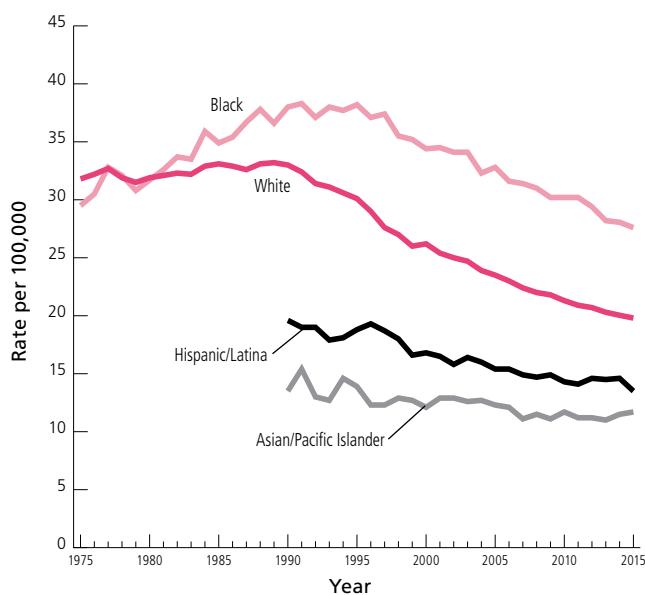
Figure 6a. Trends in Female Breast Cancer Incidence Rates by Race/Ethnicity, 1975-2014, US



Note: Rates are age adjusted to the 2000 US standard population and adjusted for reporting delays.

Source: SEER Program, National Cancer Institute, 2017. Data for whites and blacks are from the 9 SEER registries and data for other races/ethnicities are 3-year moving averages from the 13 SEER registries. For Hispanics, incidence data do not include cases from the Alaska Native Registry. Data for AI/AN not shown due to small counts and unstable rates.

Figure 6b. Trends in Female Breast Cancer Death Rates by Race/Ethnicity, 1975-2015, US

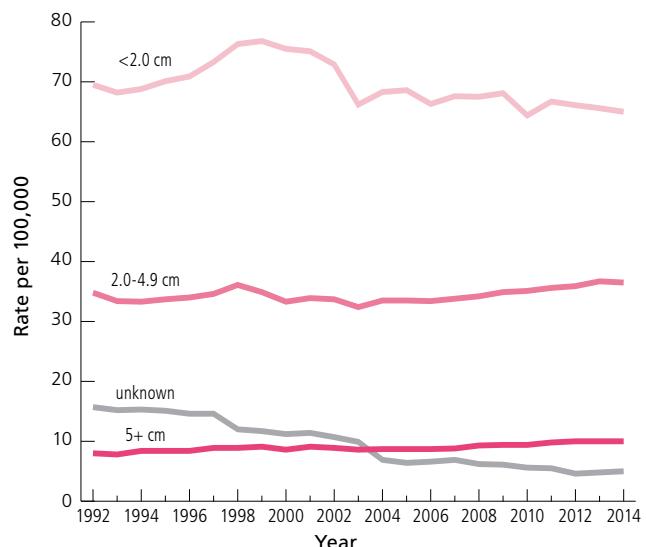


Note: Rates are age adjusted to the 2000 US standard population.

Source: National Center for Health Statistics, Centers for Disease Control and Prevention, 2017. Rates for Hispanics exclude deaths from Louisiana, New Hampshire, and Oklahoma. Data for AI/AN not shown due to small counts and unstable rates.

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Figure 7. Trends in Female Breast Cancer Incidence Rates by Tumor Size, 1992-2014, US



Note: Rates are age adjusted to the 2000 US standard population and adjusted for reporting delays.

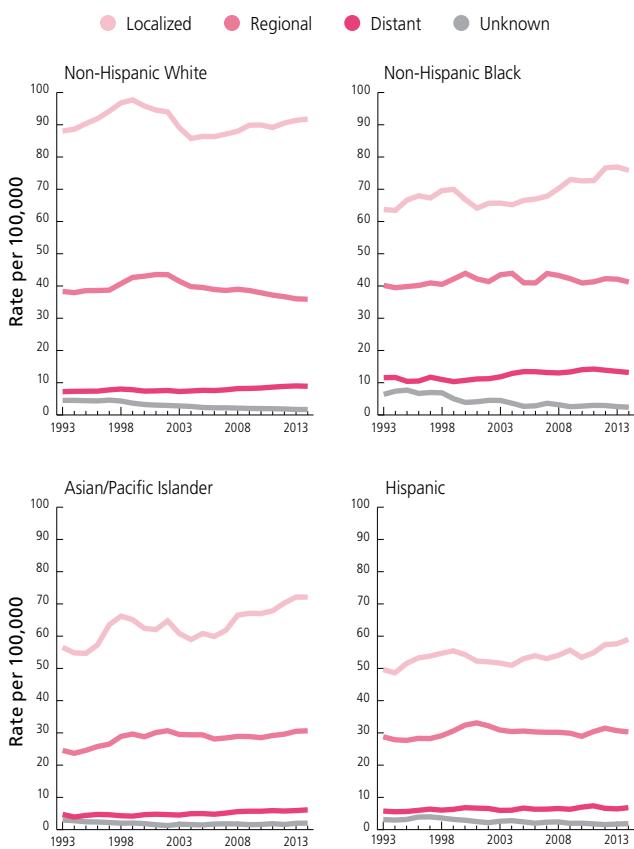
Source: 13 SEER Registries, National Cancer Institute, 2017.

American Cancer Society, Inc., Surveillance Research, 2017

AI/ANs, 1.8% in NHWs, 1.5% in NHBs, 1.4% in Hispanics, and 0.9% in APIs.¹⁷ Notably, the decline among AI/AN women began in 2005, more than a decade later than other racial and ethnic groups.

The decline in breast cancer mortality has been attributed to both improvements in treatment and early detection.²³ However, not all women have benefited equally, as indicated by the striking divergence in mortality trends between black and white women beginning in the early 1980s (Figure 6b). This disparity likely reflects a combination of factors, including differences in stage at diagnosis, obesity and comorbidities, and tumor characteristics, as well as access, adherence, and response to treatment.²⁴⁻²⁷ It may also reflect differences in mammography screening. Although findings from national surveys indicate current screening rates are similar between black and white women, these estimates likely overestimate mammography rates, especially for blacks.²⁸⁻³⁰ As treatment for breast cancers has improved, the racial disparity widened; in 2015, breast cancer death rates were 39% higher in black than white women.

Figure 8. Trends in Female Breast Cancer Incidence Rates by Stage and Race/Ethnicity, 1992-2014, US



Note: Rates are two year moving averages, age adjusted to the 2000 US standard population, and adjusted for reporting delay.

Source: 13 SEER Registries, National Cancer Institute, 2017.

American Cancer Society, Inc., Surveillance Research, 2017

Relative survival rates should be interpreted with caution. First, they are based on the average experience of all women and do not predict individual prognosis because many patient and tumor characteristics that influence breast cancer survival are not taken into account. Second, long-term survival rates are based on the experience of women diagnosed and treated many years ago and do not reflect the most recent improvements in early detection and treatment.

Stage at diagnosis

Breast cancer survival varies by stage at diagnosis (Figure 9a). The overall 5-year relative survival rate is 99% for localized disease, 85% for regional disease, and 27% for distant-stage disease.¹⁷ Survival within each stage varies by tumor size. For example, among women with regional disease, the 5-year relative survival is 95% for tumors less than or equal to 2.0 cm, 85% for tumors 2.1-5.0 cm, and 72% for tumors greater than 5.0 cm.³¹

Race/ethnicity and socioeconomic factors

Since 1975, the breast cancer 5-year relative survival rate has increased significantly for both black and white women (Figure 10). While there remains a substantial gap, especially for late-stage diagnoses, the racial disparity seems to be narrowing. In the most recent period, the 5-year relative survival rate was 83% for black women and 92% for white women. The racial disparity in survival reflects later stage at diagnosis and poorer stage-specific survival in black women as well as higher rates of more aggressive, triple negative breast cancer.

Cause-specific survival instead of relative survival is used to describe the cancer experience of racial and ethnic minorities because reliable life expectancy is not available for some groups. Cause-specific survival is the probability of not dying of breast cancer within five years of diagnosis. For every stage of disease, API women have the highest survival and NHB women have the lowest survival (Figure 9). Poverty, less education, and a lack of health insurance are associated with lower breast cancer survival.³²⁻³⁶

Breast cancer survival

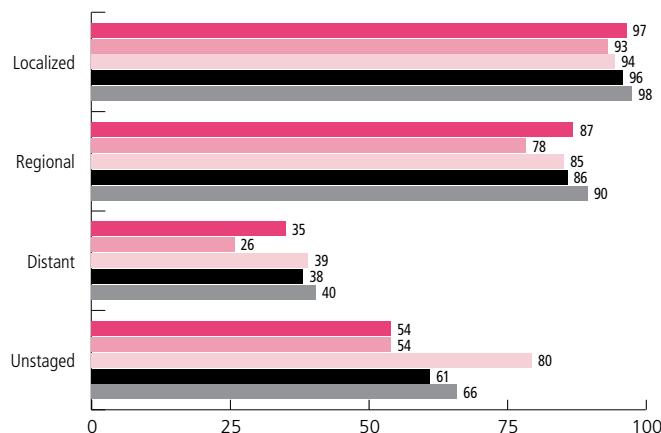
Relative survival rates are an estimate of the percentage of patients who will survive for a given period of time after a cancer diagnosis, accounting for normal life expectancy. Survival among cancer patients is compared to survival among people of the same age and race who have not been diagnosed with cancer.

Based on the most recent data, relative survival rates for women diagnosed with breast cancer are:

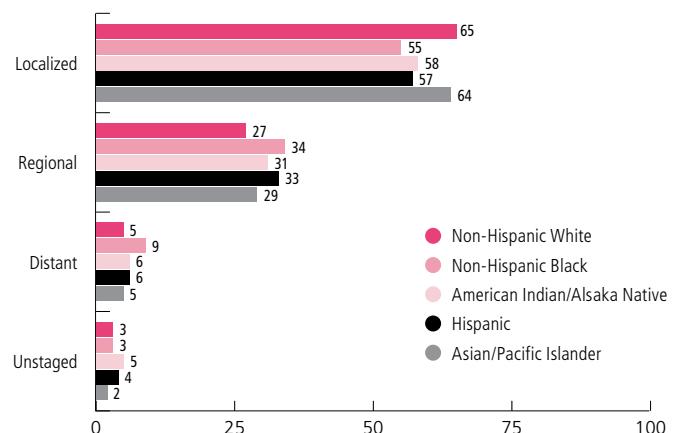
- 91% at 5 years after diagnosis
- 86% after 10 years
- 80% after 15 years

Figure 9. Female Breast Cancer-specific Survival and Stage Distribution by Race/Ethnicity, 2007-2013, US

a. Five-year Breast Cancer-specific Survival Rates (%)



b. Stage Distribution (%)



Survival rates are based on patients diagnosed during 2007-2013 and followed through 2014. Stage distribution percentages may not sum to 100 due to rounding.

Sources: Survival – SEER Program, 18 SEER registries, National Cancer Institute, 2016. Stage distribution – NAACCR, 2017.

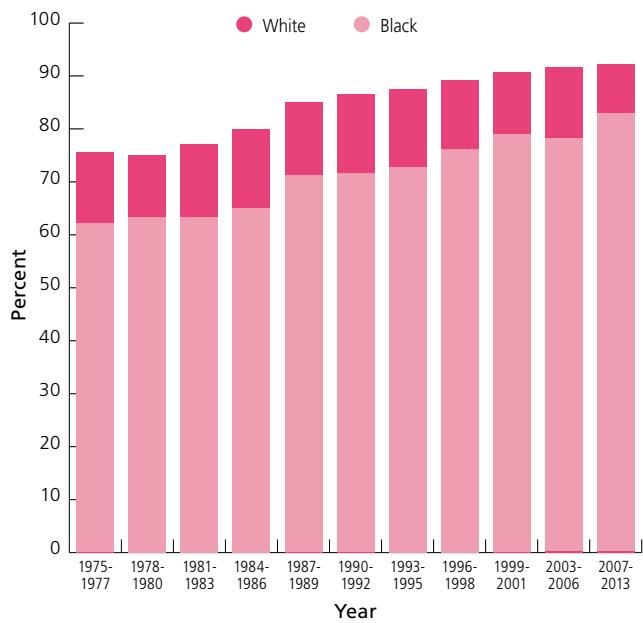
American Cancer Society, Inc., Surveillance Research, 2017

Male breast cancer

Breast cancer in men is rare, accounting for less than 1% of breast cancer cases in the US. However, since 1975, the incidence rate has increased slightly, from 1.0 case per 100,000 men during 1975-1979 to 1.3 cases per 100,000 men during 2010-2014. Men are more likely than women to be diagnosed with advanced-stage breast cancer, which likely reflects decreased awareness and delayed detection because screening mammography is not recommended for men due to the rarity of the disease.³⁷ Similar to female breast cancer, the incidence of male breast cancer increases with age. The death rate for male breast cancer has decreased slightly from 0.4 (per 100,000) during 1975-1979 to 0.3 (per 100,000) during 2011-2015 due to improvements in treatment.

Due to the infrequency of male breast cancer, much less is known about the disease than female breast cancer. Risk factors include radiation exposure, *BRCA 1/2* gene mutations, Klinefelter syndrome, testicular disorders, family history of breast or ovarian cancer, diabetes, gynecomastia (enlarged breasts), and obesity.^{38,39}

Figure 10. Trends in Female Breast Cancer 5-year Relative Survival Rates by Race, 1975-2013, US



Survival rates are based on follow-up of patients through 2014.

Source: Howlader et al.¹⁷

American Cancer Society, Inc., Surveillance Research, 2017

Breast Cancer Risk Factors

About one-third of postmenopausal breast cancers are thought to be caused by behavioral factors that are modifiable, such as postmenopausal obesity, physical inactivity, use of combined estrogen and progestin menopausal hormones, alcohol consumption, and not breastfeeding.⁴⁰ Many risk factors affect lifetime exposure of breast tissue to hormones (early menarche, late menopause, obesity, and hormone use). Hormones are thought to influence breast cancer risk by increasing cell proliferation, thereby increasing the likelihood of DNA damage, as well as promoting cancer growth. Although exposures that influence risk accumulate throughout a woman's life, research suggests that the time between menarche and first pregnancy may be particularly critical.^{41, 42} Many established risk factors for breast cancer are specifically associated with HR+/luminal breast cancer; less is known about risk factors for HR-, HER2+ or basal-like breast cancers.⁴³ Factors associated with an increased or decreased risk of breast cancer are discussed below.

Family history and personal characteristics

Family history

Women and men with a family history of breast cancer, especially in a first-degree relative (parent, child, or sibling), are at increased risk for the disease. Compared to women without a family history, risk of breast cancer is about 2 times higher for women with one affected first-degree female relative and 3-4 times higher for women with more than one first-degree relative.⁴⁴ Risk is further increased when the affected relative was diagnosed at a young age or if the cancer was diagnosed in both breasts. It is important to note that the majority of women with one or more affected first-degree relatives will never develop breast cancer and that most women who develop breast cancer do not have a family history of the disease.

A family history of ovarian cancer is also associated with increased breast cancer risk in both men and women.

Women with a family history of breast or ovarian cancer should discuss this with their physician or a genetic counselor because it may signal the presence of a genetic predisposition to cancer.

Genetic predisposition

Inherited mutations (genetic alterations) in *BRCA1* and *BRCA2*, the most well-studied breast cancer susceptibility genes, account for 5%-10% of all female breast cancers, 5%-20% of male breast cancer, and 15%-20% of all familial breast cancers.^{45, 46} These mutations are rare (much less than 1%) in the general population, but occur slightly more often in certain ethnic or geographically isolated groups, such as those of Ashkenazi (Eastern European) Jewish descent (about 2%).⁴⁷ Compared to women in the general population who have a 10% risk of developing breast cancer by 80 years of age, the corresponding risks for *BRCA1* and *BRCA2* mutation carriers are estimated to be as much as 70%.⁴⁸ Mutations in *PALB2*, a different gene that works with *BRCA2*, appear to confer risk that may be as high as *BRCA2* mutations.⁴⁹

Other inherited conditions associated with a smaller increase in breast cancer risk include the Li-Fraumeni and Cowden syndromes.⁴⁵ In addition, more than 150 less rare genetic variants are associated with slightly elevated risk.⁵⁰ Scientists now believe that much of the occurrence of breast cancer clustered in families results from the interaction between lifestyle factors and these low-risk variations.⁵¹

The US Preventive Services Task Force recommends primary care providers routinely collect and update family medical history and screen women with a family history of breast, ovarian, tubal, or peritoneal cancer with one of several brief questionnaires to determine if there is a need for in-depth genetic counseling to consider *BRCA* testing.⁵² Those who consider testing are strongly encouraged to talk with a genetic counselor before making a decision so that the benefits and potential consequences can be understood and carefully considered.

Personal history of breast cancer

Women diagnosed with breast cancer have a small increased risk of developing a new cancer in the opposite breast; however, rates of second breast cancers have declined steadily since 1985.⁵³ The decrease has predominantly been among ER+ breast cancer patients and may reflect the effect of hormone therapy (e.g., tamoxifen and aromatase inhibitors) or other adjuvant treatments.⁵⁴

DCIS and LCIS

DCIS is considered a potential precursor to invasive cancer, and is also associated with an increased risk for developing a new invasive breast cancer. Women with a history of DCIS are about 10 times more likely to be diagnosed with an invasive breast cancer than women without DCIS.⁵⁵

Although LCIS seldom becomes invasive cancer, it is a strong indicator of increased risk. Women with LCIS are 7 to 12 times more likely to develop invasive cancer in either breast than women without LCIS.⁵⁶ Women with LCIS have been estimated to have a 2% annual risk of being diagnosed with invasive breast cancer.⁵⁷

Benign breast disease

Doctors often categorize benign breast conditions into 3 general groups reflecting the associated degree of cancer risk: nonproliferative lesions, proliferative lesions without atypia (abnormal cells or patterns of cells), and proliferative lesions with atypia.

- Nonproliferative lesions are not associated with overgrowth of breast tissue and include fibrosis and simple cysts (also known as fibrocystic changes) and mild hyperplasia. Nonproliferative conditions are associated with little to no increased breast cancer risk.⁵⁸
- Proliferative lesions without atypia are associated with a small increase in the risk of breast cancer (1.5 to 2 times the risk of those who do not have one of these lesions) and include usual ductal hyperplasia (without atypia) and fibroadenoma.⁵⁸

Table 4. Factors That Increase the Relative Risk for Breast Cancer in Women

Relative Risk	Factor
>4.0	Age (65+ versus <65 years, although risk increases across all ages until age 80) Biopsy-confirmed atypical hyperplasia Certain inherited genetic mutations for breast cancer (<i>BRCA1</i> and/or <i>BRCA2</i>) Ductal carcinoma in situ Lobular carcinoma in situ Mammographically dense breasts (compared to least dense) Personal history of early-onset (<40 years) breast cancer Two or more first-degree relatives with breast cancer diagnosed at an early age
2.1-4.0	Personal history of breast cancer (40+ years) High endogenous estrogen or testosterone levels (postmenopausal) High-dose radiation to chest One first-degree relative with breast cancer
1.1-2.0	Alcohol consumption Ashkenazi Jewish heritage Diethylstilbestrol exposure Early menarche (<12 years) Height (tall) High socioeconomic status Late age at first full-term pregnancy (>30 years) Late menopause (>55 years) Never breastfed a child No full-term pregnancies Obesity (postmenopausal)/adult weight gain Personal history of endometrium or ovarian cancer Proliferative breast disease without atypia (usual ductal hyperplasia and fibroadenoma) Recent and long-term use of menopausal hormone therapy containing estrogen and progestin Recent oral contraceptive use

- Proliferative lesions with atypia are associated with about 4 times higher than average risk. These include atypical ductal hyperplasia and atypical lobular hyperplasia.⁵⁸

Benign breast conditions are most strongly associated with risk for HR+ breast cancers. Women should keep detailed records of any benign breast biopsy results, as they are valuable for risk assessment, screening, and counseling for chemoprevention and other risk-reduction strategies.

Breast density

Breast tissue density is a mammographic indicator of the amount of glandular and connective tissue relative to fatty tissue. Compared to women with 11%-25% breast density, those with 26%-50% or 50% or greater breast density have about a 1.6 or 2.3 times, respectively, higher risk of breast cancer.⁵⁹ About 43% of US women ages 40-74 have heterogeneously dense or extremely dense breasts (BI-RADS C or D).⁶⁰ Breast density is influenced by genetics, but generally decreases with age, pregnancy, menopause, and higher body weight.^{61,62} Some drugs also affect breast density, including tamoxifen (decreases density) and combined menopausal hormone therapy (increases density).^{63,64}

Mammographic detection of breast cancer is impaired in areas of dense breast tissue.⁶⁵ More than half of US states now have laws requiring that mammography reports include information about breast density.⁶⁶ Many states with these laws also require that women with dense breasts be told that they may benefit from supplemental imaging tests, such as ultrasound or MRI. Digital breast tomosynthesis is also useful in evaluating dense breasts. However, there is currently no expert consensus about what other tests, if any, should be done in addition to mammograms to screen for breast cancer in women with dense breasts.^{67,68}

Height

Many studies have found that taller women have a higher risk of breast cancer than shorter women.^{69,70} A recent study from Europe found that an increase of 2 inches in height was associated with about a 10% higher risk of breast cancer diagnosis and death.⁷¹ Height is also associated with a number of other cancers, and although the reasons are not fully understood, it may reflect differences in early growth as well as hormonal or genetic factors.

Menstrual cycles

Breast cancer risk increases slightly for each year earlier menstruation begins (by about 5%) and for each year later menopause begins (by about 3%).⁷² For example, breast cancer risk is about 20% higher among girls who begin menstruating before age 11 compared to those who

begin at age 13.⁷² Likewise, women who experience menopause at age 55 or older have about a 12% higher risk compared to those who do so between ages 50-54.⁷² The increased risk may be due to longer lifetime exposure to reproductive hormones and has been more strongly linked to HR+ breast cancer than other subtypes.⁷³

Bone mineral density

High bone mineral density in postmenopausal women has been associated with a 60% to 80% increased risk for breast cancer compared to low bone density; risk appears to be most strongly related to HR+ disease.^{74,75} Bone density is not thought to be an independent risk factor for breast cancer, but a marker of cumulative estrogen exposure.⁷⁶ However, because bone density is routinely measured to identify women at increased risk for osteoporosis (high bone density indicates absence of osteoporosis), it also may be helpful for identifying women at increased risk for breast cancer.

Endogenous hormone levels

Postmenopausal women with naturally high levels of certain endogenous sex hormones have about twice the risk of developing breast cancer compared to women with the lowest levels, with the strongest relationships found for HR+ tumors.^{77,78} High circulating hormone levels are associated with, and may reflect, the effects of other breast cancer risk factors, such as postmenopausal obesity and alcohol use.⁷⁸ Although it is challenging to study the relationship of hormones in premenopausal women because levels vary across the menstrual cycle, a recent large review found that high levels of circulating estrogens and androgens are associated with a small increased risk of breast cancer in premenopausal women.⁷⁹

Reproductive factors

Pregnancy

Having a first child before age 35 and having a greater number of children is associated with decreased risk of HR+ breast cancer.⁸⁰ In contrast, there appears to be a transient increase in HR- breast cancer risk (lasting about 10 years) following a full-term pregnancy, particularly among women who are older at first birth.^{81,82}

Fertility drugs

More research is needed on the relationship between breast cancer risk and the long-term effects of ovulation-stimulating drugs.⁸³ A long-term follow-up study of women seen at 5 US fertility clinics found no association with ever use of clomiphene or gonadotropins; however, risk of invasive breast cancer was increased among women who underwent more than 12 clomiphene treatment cycles compared to women who had never used fertility drugs.⁸⁴ Recently published results of a long-term follow-up study of Dutch women who used fertility drugs for in vitro fertilization (IVF), found no overall association of breast cancer risk with IVF and a significantly reduced risk of breast cancer among women who had undergone seven or more IVF cycles.⁸⁵

Breastfeeding

Most studies suggest that breastfeeding for a year or more slightly reduces a woman's overall risk of breast cancer, with longer duration associated with greater risk reduction.⁸⁶ In a review of 47 studies in 30 countries, the risk of breast cancer was reduced by 4% for every 12 months of breastfeeding.⁸⁷ One possible explanation for this effect may be that breastfeeding inhibits menstruation, thus reducing the lifetime number of menstrual cycles.⁸⁸ Another possible explanation relates to structural changes that occur in the breast following lactation and weaning.⁸⁶ The protective effect may be stronger for or even limited to triple negative cancers.^{86, 89-90}

Hormonal birth control

Studies suggest that recent use of oral contraceptives (combined estrogen and progestin) is associated with a small increase in breast cancer risk, particularly among women who begin use before 20 years of age or before first pregnancy.⁹¹ Risk appears to diminish when women stop use, and after about 10 years, is similar to those who have never taken oral contraceptives. Most of this research considered high-dose estrogen formulations, which were more common in the past. It is unclear if newer, low-dose estrogen formulations increase breast cancer risk.

Some, but not all, studies have found recent use of the injectable progestin-only contraceptive depot-medroxyprogesterone acetate (Depo-Provera) to be associated with increased risk of breast cancer; however, no association has been found with prior use (5 or more years ago).⁹²⁻⁹⁴ Studies of the levonorgestrel-releasing intrauterine device (Mirena) have also produced conflicting results.⁹⁵⁻⁹⁸ Depo-Provera and Mirena have only been in use since the 1990s, thus studies with additional years of follow-up data are needed. Importantly, overall breast cancer risk is low in young women, and most studies suggest that any elevation in risk is temporary.

Postmenopausal hormones

Recent use of menopausal hormones (also referred to as hormone therapy or hormone replacement therapy) with combined estrogen and progestin increases the risk of breast cancer, with higher risk associated with longer use.^{99, 100} Risk is also greater for women who start hormone therapy soon after the onset of menopause compared to those who begin later.^{99, 101} Although discontinuation of hormone use diminishes breast cancer risk, some increase in risk seems to persist.¹⁰² The increased risk associated with estrogen and progestin therapy may be largely due to increased mammographic density.⁶⁵

Postmenopausal estrogen-only therapy has been associated with uterine problems (including endometrial cancer), and is therefore only given to women who have previously undergone hysterectomy. The effects of estrogen-only therapy on breast cancer risk is less clear. The US Preventive Services Task Force has concluded that the use of estrogen alone is associated with reduced risk of breast cancer based on results from the Women's Health Initiative randomized trial, which found that women who used estrogen-only therapy for an average of 6 years had a 23% lower risk of developing breast cancer.¹⁰⁴ It should be noted, however, that some observational studies have found a slight increase in breast cancer risk among estrogen therapy users, particularly among lean women and those who begin therapy soon after menopause.^{101, 105, 106} Conflicting results may reflect higher rates of screening in menopausal hormone users, which were not controlled for in the observational studies.¹⁰⁷

Obesity, physical activity, and diet

Obesity and weight gain

Postmenopausal breast cancer risk is about 1.5 times higher in overweight women and about 2 times higher in obese women than in lean women.¹⁰⁸ This is likely due, in part, to higher estrogen levels because fat tissue is the largest source of estrogen in postmenopausal women, but may also be related to other mechanisms, including the higher levels of insulin among obese women.^{109, 110} Obesity is a risk factor for type II diabetes, which has also been linked to increased risk for postmenopausal breast cancer.^{111, 112} A review of 40 studies concluded that breast cancer risk was 16% higher in women with type II diabetes independent of obesity.¹¹³

Weight gain also increases risk of postmenopausal breast cancer. A large meta-analysis recently concluded that each 5 kg (about 11 pounds) gained during adulthood increases risk of postmenopausal breast cancer by 11%.¹¹⁴ Notably, the increased risk was only observed among women who did not use menopausal hormones. Although some studies have found weight loss to be associated with reduced risk, results are inconsistent.¹¹⁵⁻¹¹⁷ It is more difficult to examine the effect of weight loss because it is often not sustained.

In contrast, studies have found that obesity protects against premenopausal breast cancer. A large meta-analysis found that among women between 40 and 49 years of age, the risk for developing breast cancer was about 14% lower in overweight women and 26% lower in obese women compared to women who were normal weight.¹¹⁸ The underlying mechanisms for this inverse relationship are not well understood, but the protective effect may be limited to HR+/luminal A breast cancers.⁴³

Physical activity

Women who get regular physical activity have a 10%-20% lower risk of breast cancer compared to women who are inactive.¹¹⁹ The protective effect is independent of BMI and may be limited to women who have never used menopausal hormone therapy.¹¹⁹ A greater reduction in risk is associated with increasing amounts of exercise and more vigorous activity; however, even smaller amounts of

What is the difference between absolute, lifetime, and relative risks?

Absolute risk: Absolute risk is the likelihood of being diagnosed with cancer over a certain period of time. For example, 22 out of 10,000 women ages 50-54 will be diagnosed with breast cancer in the next year.

Lifetime risk: Lifetime risk is the absolute risk of being diagnosed with cancer over the course of a lifetime from birth to death. Lifetime risk of breast cancer reflects the average probability of a female being diagnosed with breast cancer in the US. A woman living in the US has a 12% chance of being diagnosed with breast cancer in her lifetime (Table 2, page 4). Another way to say this is that 1 out of every 8 women will be diagnosed with breast cancer in her lifetime.

Relative risk: Relative risk compares the absolute risk of disease among people with a particular risk factor to the risk among people without that risk factor. If the relative risk is above 1.0, then risk is higher among those with the risk factor than among those without the factor. Relative risks below 1.0 reflect an inverse association between the exposure and the disease, or a protective effect. For example, one study found women ages 50-59 who were current users of combined estrogen and progestin menopausal hormones had a relative risk of developing breast cancer of 1.21, or a 21% increased risk compared to women who have not used hormone therapy.¹⁰⁰ While relative risks are useful for comparisons, they do not provide information about the absolute risk of the exposed group. In this example, 33 breast cancers per year would be expected to be diagnosed among 10,000 women ages 50-59 who use estrogen and progestin (that is the absolute risk among this group). Among 10,000 women of the same ages who never used menopausal hormones, 27 cases per year would be expected. Therefore, the 21% increased relative risk results in a total of 6 additional breast cancers diagnosed per 10,000 women per year.

exercise, including walking, appear beneficial.¹²⁰ An American Cancer Society study that included more than 73,000 postmenopausal women found that breast cancer risk was 14% lower among women who reported walking 7 or more hours per week compared to women who walked 3 or less hours per week.¹²⁰ The benefit may be due to the effects of physical activity on systemic inflammation, hormones, and energy balance.^{119, 121}

Diet

Numerous studies have examined the relationship between food consumption (including fat, fiber, soy, dairy, meat, and fruits and vegetables) and breast cancer with mixed results. Although early diet and breast cancer studies focused on fat intake, a recent meta-analysis concluded there was no association.¹²² It has been suggested that soy consumption may reduce breast cancer risk, in part because of historically low breast cancer rates among Asian women. A meta-analysis showed that soy intake was inversely associated with breast cancer risk in Asian but not Western populations, perhaps because Asian women generally consume more soy products beginning at an earlier age than Western women.¹²³

There is growing evidence that high levels of fruit and/or vegetable consumption may reduce the risk of HR- breast cancer.¹²⁴⁻¹²⁶ These findings are supported by studies linking lower breast cancer risk to higher blood levels of carotenoids (micronutrients found in fruit and vegetables).¹²⁷⁻¹²⁹ The effect of diet on breast cancer risk remains an active area of research, with studies particularly focused on timing of exposure, specific dietary components, and risk differences by tumor hormone receptor status.

Alcohol

Numerous studies have confirmed that alcohol consumption increases the risk of breast cancer in women by about 7%-10% for each 10g (roughly one drink) of alcohol consumed per day on average.⁴¹ Women who have 2-3 alcoholic drinks per day have a 20% higher risk of breast cancer compared to non-drinkers. There is also evidence that alcohol consumption before first pregnancy may particularly affect risk.^{41, 130} One of the mechanisms by which alcohol increases risk is by increasing estrogen and androgen levels.¹³¹ Alcohol use appears more strongly associated with increased risk for HR+ than HR- breast cancers.¹³²

Tobacco

Accumulating research indicates that smoking may slightly increase breast cancer risk, particularly long-term, heavy smoking and among women who start

smoking before their first pregnancy.¹³³⁻¹³⁶ The 2014 US Surgeon General's report on smoking concluded that there is "suggestive but not sufficient" evidence that smoking increases the risk of breast cancer.¹³⁷ A review by American Cancer Society researchers found that women who initiated smoking before the birth of their first child had a 21% higher risk of breast cancer than women who never smoked.¹³⁵ Some studies suggest secondhand smoke may increase risk, particularly for premenopausal breast cancer.^{133, 134}

Environmental and other risk factors

Radiation

Radiation exposure has been shown to increase breast cancer risk in studies of atomic bomb survivors and females treated with high-dose radiation therapy to the chest between 10 and 30 years of age, such as for Hodgkin lymphoma.^{138, 139} This may be because breast tissue is most susceptible to carcinogens before it is fully differentiated, which occurs with first childbirth.¹⁴⁰ Breast cancer risk starts to rise about 8 years after radiation treatment and continues to be elevated for more than 35 years.^{139, 141} Although radiation treatments have evolved to include lower doses given over smaller areas, recent studies suggest that the elevated breast cancer risk persists.^{141, 142}

Diethylstilbestrol exposure

From the 1940s through the 1960s, some pregnant women were given the drug diethylstilbestrol (DES) because it was thought to lower the risk of miscarriage. These women have an increased risk (about 30%) of developing breast cancer compared to women who have not taken DES.¹⁴³ Some studies also suggest that women whose mothers took DES during pregnancy also have a slightly higher risk of breast cancer.¹⁴⁴

Environmental pollutants

In general, epidemiological studies have not found clear relationships between environmental pollutants, such as organochlorine pesticides, and breast cancer. Studies to date have found no association between increased concentrations of organochlorines (e.g., dichlorodiphenyl-

trichloroethane or DDT) in blood and fat tissue and breast cancer risk,¹⁴⁵⁻¹⁴⁸ although a recent study found in utero exposure to DDT was linked to breast cancer risk later in life.¹⁴⁹ Animal studies have demonstrated that prolonged, high-dose exposure to many industrial chemicals can increase mammary tumor development, but it is unknown whether the much lower dose exposures that occur in the general environment in air, drinking water, and consumer products increase human breast cancer risk.¹⁵⁰

Night shift work

Most studies of nurses who work night shifts and flight attendants who experience circadian rhythm disruption caused by crossing multiple time zones have found increased risks of breast cancer associated with long-term employment.^{151, 152} Elevated risk appears to be most strongly associated with shift working during early adulthood.¹⁵³ Exposure to light at night disrupts the production of melatonin, a hormone that regulates sleep. Experimental evidence suggests that melatonin may also inhibit the growth of small, established tumors and prevent new tumors from developing.¹⁵⁴ Based on the results of studies in humans and animals, the International Agency for Research on Cancer concluded in 2007 that shift work, particularly at night, was probably carcinogenic to humans.¹⁵⁵ Shift work at night is a common exposure, involving about 15% to 20% of workers in the US and Europe, and much of the population in industrialized countries is exposed to artificial light at night.

Factors that are not associated with breast cancer risk

Abortion

There are persistent claims that women who have had an abortion are at increased risk for developing breast cancer based on early studies that have since been deemed methodologically flawed by the American College of Obstetricians and Gynecology.¹⁵⁶ Indeed, a large body of solid scientific evidence, including a review by a panel of experts convened by the National Cancer Institute in 2003, confirms that there is no link between breast cancer and abortion (either spontaneous or induced).¹⁵⁷

Bras

Although internet rumors have suggested that bras cause breast cancer by obstructing lymph flow, there is no scientific basis or evidence to support this claim. A recent population-based study of more than 1,500 women found no association between wearing a bra and breast cancer.¹⁵⁸

Breast implants

No association has been found between breast implants and risk of breast cancer; however, there is evidence that women with implants are at increased risk of a rare type of lymphoma.¹⁵⁹ Breast implants can also obstruct the view of breast tissue during mammography. A woman with breast implants should inform the mammography facility about the implants during scheduling so that additional x-ray pictures (called implant displacement views) may be used to allow for more complete breast imaging.

Hair dyes, relaxers, and antiperspirants

Although one recent study suggested that selected hair products may be associated with breast cancer, most studies have failed to reveal any correlation.¹⁶⁰ A combined analysis of 14 studies found no association between the use of permanent hair dyes and breast cancer.¹⁶¹ A study of more than 48,000 black women found no link to breast cancer with use of hair relaxers.¹⁶² Although antiperspirant use has been less well-studied, there is presently no convincing scientific evidence of an association with breast cancer.^{163, 164}

Chemoprevention and prophylactic surgery

Chemoprevention

The use of drugs to reduce the risk of disease is called chemoprevention. Currently, the US Food and Drug Administration (FDA) has approved two drugs for the prevention of breast cancer in high-risk women: tamoxifen and raloxifene (postmenopausal women only). These drugs are classified as selective estrogen receptor modulators (or SERMs) because they block estrogen in some tissues of the body, but act like estrogen in others. A recent meta-analysis, including more than 83,000 high-risk women, found that SERMs reduced breast

cancer risk by 38% over 10 years.¹⁶⁵ Although the benefit is limited to ER+ disease, these drugs lower the risk of both invasive cancer and ductal carcinoma in situ. However, SERMs are associated with some side effects, including hot flashes, nausea, and fatigue. Premenopausal women taking tamoxifen can also experience menstrual changes. More serious side effects are rare, but include blood clots and endometrial cancer.¹⁶⁵

Clinical trials are examining another class of drugs – aromatase inhibitors – to see if they may also be effective for reducing breast cancer risk among postmenopausal women. Currently, these drugs are only approved to prevent breast cancer recurrence. Aromatase inhibitors target the enzyme responsible for producing estrogen in fat tissue, and thus are only effective in women without functioning ovaries (e.g., postmenopausal women), because ovaries are the primary source of estrogen before menopause. Early clinical trial results are promising: breast cancer risk was reduced by more than half in high-risk women taking anastrozole or exemestane compared to placebo.^{166, 167} Women taking aromatase

inhibitors must be monitored for osteoporosis, as these medications can decrease bone density.

Prophylactic surgery

Women at very high risk of breast cancer (such as those with *BRCA* gene mutations) may elect prophylactic (preventive) mastectomy. This operation removes one or both breasts. Removing both breasts before cancer is diagnosed reduces the risk of breast cancer by 90% or more.¹⁶⁸ Prophylactic salpingo-oophorectomy (surgical removal of the fallopian tubes and ovaries) has also been shown to reduce the risk of both breast and ovarian cancers,^{169, 170} but a recent study found that the breast cancer benefit may be limited to women who carry *BRCA2* mutations.¹⁷¹ Importantly, however, not all women who elect to have these surgeries would have developed cancer. A woman considering prophylactic surgery should discuss the benefits and limitations with her doctor and a second opinion is strongly recommended. See page 25 for further discussion of contralateral prophylactic mastectomy.

Breast Cancer Screening

American Cancer Society recommendations for the early detection of breast cancer vary depending on a woman's age and include mammography, as well as magnetic resonance imaging (MRI) for women at high risk. In 2015, the American Cancer Society updated its breast cancer screening guideline for average-risk women.¹⁷²

Mammography

Mammography is a low-dose x-ray procedure that allows visualization of the internal structure of the breast. There are three main types of mammography: screen-film, digital, and digital breast tomosynthesis. Screen-film mammography uses x-ray equipment to record images. Digital mammography, which uses more specialized computerized equipment to capture a digital image of the breast and delivers lower doses of radiation, has largely replaced film mammography. Studies have shown that

digital mammograms are more accurate for women under the age of 50 and those with dense breast tissue.¹⁷³⁻¹⁷⁵

In 2011, the FDA approved the use of digital breast tomosynthesis or 3-dimensional (3-D) mammography, which constructs a 3-D image of the breast with multiple high-resolution x-rays, to be used in combination with a 2-D digital mammography image. The benefits and limitations of tomosynthesis in community practice are still being assessed. Recent studies suggest that the addition of breast tomosynthesis to digital mammography may reduce false positives and slightly improve cancer detection compared to digital mammography alone.¹⁷⁶⁻¹⁷⁸ However, when the 2-D images are produced separately from the tomographic images, women receive about twice the radiation dose. Recently, the FDA approved the use of tomographic images to produce synthetic, conventional 2-D images, thus reducing the radiation dose to that similar to conventional digital mammography. This

newer type of mammographic screening is not yet available in all communities and may not be fully covered by health insurance.

For women at average-risk of breast cancer, the American Cancer Society recommends that those 40 to 44 years of age have the option to begin annual mammography; those 45 to 54 years should undergo annual mammography; and those 55 years of age or older may transition to biennial mammography or continue with annual mammograms. Women should continue screening as long as their overall health is good and they have a life expectancy of 10 years or more.

It is especially important that women are regularly screened to increase the chance that a breast cancer is detected early before it has spread. Recommended screening intervals are based on the duration of time a breast cancer is detectable before symptoms develop. Combined results from randomized controlled screening trials suggest that mammography reduces the risk of dying from breast cancer by about 20%, whereas studies of modern mammography screening programs in Europe and Canada found that the risk of breast cancer death among women exposed to screening was reduced by more than 40%.¹⁷⁹⁻¹⁸¹ Early detection of breast cancer by mammography also leads to a greater range of treatment options, including less-extensive surgery (e.g., breast-conserving surgery like lumpectomy versus mastectomy) and the use of chemotherapy with fewer serious side effects, or sometimes, the option to forgo chemotherapy. However, mammography screening does have limitations or potential harms, which are described below.

The Affordable Care Act requires that Medicare and all new health insurance plans fully cover screening mammograms without any out-of-pocket expense for patients. For help locating a free or low-cost screening mammogram in your area, contact the American Cancer Society at 1-800-227-2345.

False-positive results

Mammography sometimes leads to follow-up examinations, including biopsies, when there is no cancer, referred to as false-positive test results. A false

American Cancer Society Guideline for Breast Cancer Screening, 2015¹⁷²

These recommendations represent guidance from the American Cancer Society for women at average risk of breast cancer, i.e., women without a personal history of breast cancer, a suspected or confirmed genetic mutation known to increase risk of breast cancer (e.g., *BRCA*), or a history of previous radiotherapy to the chest at a young age.

We recommend that all women should become familiar with the potential benefits, limitations, and harms associated with breast cancer screening.

Recommendations:*

1. Women with an average risk of breast cancer should undergo regular screening mammography starting at age 45 years (strong recommendation).
 - Women should have the opportunity to begin annual screening between the ages of 40 and 44 (qualified recommendation).
 - Women who are age 45 to 54 should be screened annually (qualified recommendation).
 - Women who are age 55 and older should transition to biennial screening or have the opportunity to continue screening annually (qualified recommendation).
2. Women should continue screening mammography as long as their overall health is good and they have a life expectancy of 10 years or more (qualified recommendation).
3. The American Cancer Society does not recommend clinical breast examination for breast cancer screening among average-risk women at any age (qualified recommendation).

*A strong recommendation conveys the consensus that the benefits of adherence to that intervention outweigh the undesirable effects that may result from screening. Qualified recommendations indicate there is clear evidence of the benefit of screening but less certainty about either the balance of benefits and harms, or about patients' values and preferences, which could lead to different decisions about screening.

positive is most likely following a woman's initial screening mammogram.¹⁸² Other factors that increase the likelihood of a false positive include the use of postmenopausal hormone therapy and having more

mammographically dense breast tissue.^{182, 183} On average, 1 in 9 women are recalled from each screening examination for further testing (most often additional mammographic views), but most (95%) do not have cancer.¹⁸⁴ According to one US study, over the course of 10 screening examinations, about one-half of women experience a false positive, and about 19% undergo biopsy but do not have cancer.¹⁸⁵

Overdiagnosis

Mammography likely results in some overdiagnosis; that is, the diagnosis of cancer that would not cause a woman any harm in her lifetime and that would not have progressed or otherwise been detected in the absence of screening. There are two circumstances that can lead to overdiagnosis. The first is a breast cancer is diagnosed by screening in a woman who dies shortly afterward from a cause other than breast cancer. National guidelines recommend against screening in women who are very ill or have limited life expectancy. The second, which is more difficult to measure, is the detection of a truly non-progressive *in situ* or invasive cancer. Estimates of the prevalence of overdiagnosis are highly variable, ranging from <5% to more than 30%.¹⁸⁶⁻¹⁹¹

Radiation exposure

The dose of radiation during a mammogram is very small and the risk of harm is minimal.^{192, 193}

Limitations of mammography

Not all breast cancer will be detected early by a mammogram, and some cancers that are screen-detected still have poor prognosis. Most women will never be diagnosed with breast cancer, but will undergo regular screening and may experience one or more “false alarms.” In an effort to maximize the benefits and minimize the harms of screening, some scientists are attempting to determine which factors could be used to individualize screening recommendations (e.g., which women could start screening at older ages and/or be screened less often).¹⁹⁴

Table 5. Prevalence of Mammography (%), Women 40 and Older, US, 2015

Characteristic	Within the past year	Within the past two years
Overall	50	64
Age (years)		
40-44	38	49
45-54	54	69
55+	53	68
Race/Ethnicity		
Non-Hispanic White	50	65
Non-Hispanic Black	55	69
Asian American	47	59
American Indian and Alaska Native	46	60
Hispanic/Latina	46	61
Education		
Some high school or less	39	51
High school diploma or GED	45	58
Some college/Assoc. degree	51	66
College graduate	58	73
Sexual orientation		
Gay/Lesbian	62	78
Straight	50	64
Bisexual	*	*
Health insurance status (ages 40-64)		
Uninsured	21	31
Insured	53	68
Immigration		
Born in US	51	66
Born in US territory	47	59
In US fewer than 10 years	33	46
In US 10 or more years	47	60
Region		
Northeast	54	67
Midwest	51	63
South	50	65
West	47	63

GED = General Educational Development high school equivalency. *Estimate not provided due to instability. Note: Estimates are age adjusted to the 2000 US standard population. Mammography prevalence estimates do not distinguish between examinations for screening and diagnosis.

Source: National Health Interview Survey, 2015.

American Cancer Society, Surveillance Research, 2017

Despite these limitations, mammography is the single most effective method of early breast cancer detection since it can often identify cancer several years before physical symptoms develop. It is the position of the American Cancer Society that the balance of benefits to possible harms strongly supports the value of regular breast cancer screening in women for whom it is recommended.

Prevalence of mammography

According to the 2015 National Health Interview Survey, 50% of women 40 years of age and older reported having had a mammogram within the past year and 64% reported having a mammogram in the past 2 years (Table 5, page 21).¹⁹⁵ Among women 40 years of age and older, mammography prevalence increased from 29% in 1987 to 70% in 2000, and has since gradually declined. Women who have less than a high school education, who have no health insurance coverage, or who are recent immigrants to the US are least likely to have had a recent mammogram. Efforts to increase screening should specifically target socioeconomically disadvantaged women and recent immigrants.

Table 6 shows the percentage of US women 40 years of age and older who have had a recent mammogram by state, based on data from the 2014 Behavioral Risk Factor Surveillance System.¹⁹⁶ Among women of all races combined 40 years of age and older, reported rates of mammograms in the past 2 years range from 62% in Idaho to 82% in Massachusetts.

The Centers for Disease Control and Prevention's National Breast and Cervical Cancer Early Detection Program (NBCCEDP) was established in 1990 to improve access to breast cancer screening and diagnostic services for low-income women and was recently shown to help save lives from breast cancer.¹⁹⁷ However, the CDC estimates that the program is currently only reaching about 11% of eligible women due in part to funding shortages.¹⁹⁸

Magnetic resonance imaging (MRI)

An expert panel convened by the American Cancer Society published recommendations for the use of MRI for screening women at increased risk for breast cancer in 2007.¹⁹⁹ The panel recommended annual MRI screening in addition to mammography for women at high lifetime risk (~20%-25% or greater) beginning at 30 years of age. Women at moderately increased risk (15%-20% lifetime risk) should talk with their doctors about the benefits and limitations of adding MRI screening to their yearly mammogram. MRI screening is not recommended for

women whose lifetime risk of breast cancer is less than 15%. Studies indicate that although MRI is underutilized among high-risk women, it is often used in women who are not at high risk for breast cancer.²⁰⁰

MRI uses magnetic fields instead of x-rays to produce very detailed, cross-sectional images of the body. A contrast material (usually gadolinium) is injected into a vein to improve the ability to capture detailed images of breast tissue. It is important that screening MRIs are done at facilities that can perform an MRI-guided breast biopsy if abnormalities are found. Otherwise, the scan must be repeated at another facility if a biopsy is necessary. Although MRI is more expensive than mammography, most major insurance companies will cover some portion of the costs if a woman can be shown to be at high risk. MRIs should supplement, but not replace, mammography screening.

Breast ultrasound

Breast ultrasound is sometimes used to evaluate abnormal findings from a mammogram or physical exam. Studies have shown that ultrasound detects more cancer than mammography alone when screening women with mammographically dense breast tissue; however, it also increases the likelihood of false-positive results.^{67, 201} The use of ultrasound instead of mammograms for breast cancer screening is not recommended.

Clinical breast examination (CBE)

The American Cancer Society no longer recommends CBE for average-risk asymptomatic women based on lack of clear benefits for CBE alone or in conjunction with mammography. Compared to mammography alone, CBE plus mammography has been shown to detect only a small additional proportion of breast cancer tumors and increases the probability of false positives.^{202, 203}

Breast self-awareness

Although the American Cancer Society no longer recommends that all women perform monthly breast self-exams (BSE), all women should become familiar with both the appearance and feel of their breasts and report

Table 6. Prevalence of Mammography* (%) by State, Women 40 and Older, 2014

	Within the past year				Within the past two years			
	All	NH White	NH Black	Uninsured (Ages 40-64)	All	NH White	NH Black	Uninsured (Ages 40-64)
United States (median)*	56	56	60	27	73	72	77	43
Range	45-68	45-68	40-71	16-46	62-82	62-83	55-89	29-68
Alabama	57	55	65	27	73	71	80	39
Alaska	45	45	*	25	63	62	*	40
Arizona	54	54	55	38	71	72	74	51
Arkansas	49	49	53	21	65	65	66	29
California	60	59	71	44	77	77	89	56
Colorado	51	52	58	28	69	69	86	44
Connecticut	64	64	65	34	80	80	82	54
Delaware	63	64	63	37	79	80	78	68
District of Columbia	53	52	56	*	75	72	79	*
Florida	58	58	62	27	74	74	79	46
Georgia	60	57	67	35	75	73	81	52
Hawaii	65	62	*	34	79	76	*	52
Idaho	47	47	*	19	62	63	*	34
Illinois	55	55	56	17	74	72	79	46
Indiana	52	52	58	22	67	67	74	35
Iowa	62	62	*	28	76	76	*	37
Kansas	56	57	57	26	71	72	75	39
Kentucky	61	60	64	27	75	74	78	37
Louisiana	58	56	61	36	75	74	77	53
Maine	63	63	*	28	78	79	*	43
Maryland	63	62	70	41	79	78	84	60
Massachusetts	68	68	64	46	82	83	75	59
Michigan	58	58	59	26	76	76	80	44
Minnesota	61	61	63	39	77	77	75	56
Mississippi	53	53	58	29	68	67	71	42
Missouri	55	54	64	25	68	67	77	34
Montana	50	51	*	23	69	69	*	41
Nebraska	53	54	56	16	70	71	69	30
Nevada	52	51	40	22	70	69	54	44
New Hampshire	62	62	*	35	79	79	*	51
New Jersey	59	57	64	33	74	74	75	51
New Mexico	49	50	*	24	66	67	*	38
New York	60	59	63	40	75	74	78	53
North Carolina	63	63	65	28	77	77	78	46
North Dakota	56	57	*	33	72	73	*	43
Ohio	56	55	65	25	72	71	82	35
Oklahoma	51	52	51	23	66	66	67	37
Oregon	54	54	*	26	70	71	*	36
Pennsylvania	57	57	60	19	73	73	77	37
Rhode Island	65	66	54	34	81	81	78	47
South Carolina	54	53	59	22	72	71	77	36
South Dakota	61	61	*	27	75	75	*	48
Tennessee	56	55	61	22	73	72	78	37
Texas	54	55	58	35	71	71	76	51
Utah	49	50	*	19	66	67	*	33
Vermont	56	57	*	25	74	75	*	37
Virginia	60	58	69	31	75	74	84	51
Washington	53	54	54	20	71	72	72	32
West Virginia	56	56	50	20	72	72	71	31
Wisconsin	59	60	57	*	74	75	67	32
Wyoming	47	47	*	21	65	66	*	40

NH: non-Hispanic. *Estimate not provided due to instability.

Source: Centers for Disease Control and Prevention. Behavioral Risk Factor Surveillance System, public use data file, 2014.

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any changes promptly to their physician. Experts have concluded that self-awareness seems to be at least as effective for detecting breast cancer as structured BSE.²⁰⁴⁻²⁰⁶ If symptoms develop, women should contact a doctor immediately, even after a recent normal mammogram.

However, most lumps are not abnormal, and for women who are still menstruating, they can appear and disappear with the menstrual cycle. Most breast lumps are not cancerous.

Breast Cancer Treatment

Treatment decisions are made jointly by the patient and the physician after consideration of the stage and biological characteristics of the cancer, the patient's age, menopausal status, and preferences, and the risks and benefits associated with each option.

In Situ

Since there is no certain way to determine the progressive potential of a DCIS lesion, surgery and sometimes radiation and/or hormone therapy is the usual course of action following a diagnosis of DCIS. However, there may be a group of patients that could safely forgo surgical treatment for DCIS. Several clinical trials are underway that are comparing standard treatment to active monitoring in women with low-risk DCIS.²⁰⁷⁻²⁰⁹ Research is also ongoing to identify molecular markers of DCIS that could predict recurrence or progression to invasive cancer.²¹⁰

Classic LCIS does not require surgical treatment, but there is no consensus about optimal treatment for more aggressive (pleomorphic) LCIS.^{56, 211}

Invasive

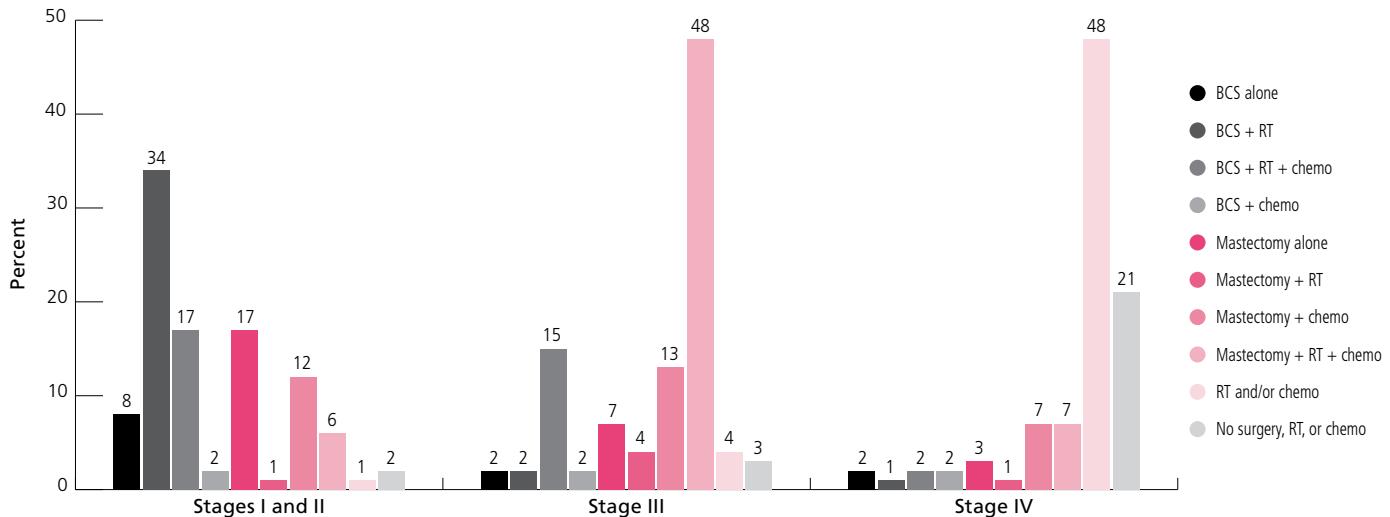
Figure 11 shows treatment patterns among US women with invasive breast cancer in 2013. Most women with early-stage breast cancer will have some type of surgery, which is often combined with other treatments to reduce the risk of recurrence, such as radiation therapy, chemotherapy, hormone therapy, and/or targeted therapy. Patients with metastatic disease are primarily treated with systemic therapies, which can include chemotherapy, targeted therapy, and hormonal therapy.

Surgery

The primary goals of breast cancer surgery are to remove the cancer and determine its stage. Surgical treatment involves breast-conserving surgery (BCS) or mastectomy. With BCS (also known as partial mastectomy or lumpectomy), only cancerous tissue, plus a rim of normal tissue (tumor margin), is removed. BCS is generally not an option in those with a high tumor-to-breast ratio, those with multicentric cancers, or those with inflammatory or locally advanced cancers. In most cases, BCS needs to be followed by radiation to the breast, and thus patients who are not candidates for breast radiotherapy, such as those who had previous breast radiation, are also not candidates for BCS. Simple or total mastectomy includes removal of the entire breast. Modified radical mastectomy includes removal of the entire breast, plus a full axillary lymph node dissection (see below for discussion of lymph node procedures). Radical mastectomy is rarely performed anymore because removal of the underlying chest muscles is not necessary to remove all of the cancer in most patients.

Long-term results of multiple international, randomized clinical trials have found equivalent survival for the majority of patients with stage I or II breast cancer who have BCS followed by radiation or mastectomy.^{212, 213} Some more recent, observational studies even suggest possible improved survival and reduced recurrence rates with BCS.²¹⁴⁻²¹⁷ In addition, risk of complications is nearly twice as high for women who undergo mastectomy with reconstruction compared to BCS plus radiation.²¹⁸ Nevertheless, many BCS-eligible women continue to undergo mastectomy.^{219, 220} Reasons include reluctance to undergo radiation therapy after BCS and fear of recurrence.²²¹ Younger women (those under 40 years of

Figure 11. Female Breast Cancer Treatment Patterns (%), by Stage, 2013, US



BCS = breast-conserving surgery; RT = radiation therapy; chemo = chemotherapy and includes targeted therapy and immunotherapy drugs.

Source: National Cancer Data Base, 2013.

American Cancer Society, Inc., Surveillance Research, 2017

age), patients with larger and/or more aggressive tumors, and those who live farther from their treatment facility are also more likely to undergo mastectomy.^{219, 221-223}

Some women who are diagnosed with breast cancer in one breast choose to have the unaffected breast removed as well. This is known as contralateral prophylactic mastectomy (CPM) or bilateral mastectomy. Recent studies have shown marked increases in the rate of CPM for women diagnosed with invasive breast cancer, as well as DCIS.^{220, 224-226} Although CPM greatly reduces the risk of developing a new breast cancer, it does not improve long-term breast cancer survival for the vast majority of women and doubles the risk of surgical complications.^{227, 228}

Both BCS and mastectomy are usually accompanied by removal of one or more regional lymph nodes from the axilla to determine if the disease has spread beyond the breast and help stage the cancer. The presence of cancer cells in the lymph nodes increases the risk of recurrence, and so can help determine the need for further treatment. Sentinel lymph node biopsy (SLNB) involves removing and testing selected lymph nodes before any others are excised. Although cancer in sentinel lymph nodes was traditionally an indication for additional axillary lymph node surgery, studies have shown that it may not be necessary when cancer cells are found only in

1 or 2 sentinel lymph nodes in patients undergoing BCS with whole breast radiation.^{229, 230} A full axillary lymph node dissection (ALND) is often indicated for patients with one or more axillary lymph nodes found to contain cancer prior to surgery. Ongoing clinical trials are investigating the safety of avoiding ALND in patients who were initially diagnosed with lymph node-positive breast cancer, but have small tumors or in whom neoadjuvant chemotherapy appears to have eliminated cancer in the lymph nodes. Patients should talk with their doctors to determine what lymph node procedure is planned for their surgery.

Surgery (and/or radiation therapy) involving the axillary lymph nodes can lead to lymphedema, a serious swelling of the arm caused by retention of lymph fluid. It affects about 20% of women who undergo ALND and 6% of patients who receive SLNB.²³¹ There are several effective therapies for lymphedema, and some evidence suggests that upper-body exercise and physical therapy may reduce the risk and lessen the severity of this condition.^{232, 233}

Women who undergo mastectomy may have breast reconstruction, either with a saline or silicone implant, tissue from another part of the body, or a combination of the two. Breast reconstruction among US women undergoing mastectomy has increased from 12% in 1998

to 36% in 2011.²²⁰ A woman considering breast reconstruction should discuss this option with her breast surgeon prior to the mastectomy in order to coordinate the treatment plan with a plastic surgeon. Some types of reconstruction can begin during the mastectomy itself, and reconstruction influences the time spent in the hospital after a procedure, as well as the recovery time. The cosmetic appearance of immediate reconstruction can be negatively affected by subsequent radiotherapy. Women who do not choose reconstruction prior to surgery can opt to undergo reconstruction later. Since 1998, the Women's Health and Cancer Rights Act has required group health plans, insurance companies, and health maintenance organizations that offer mastectomy coverage to also pay for reconstructive surgery. Reconstruction is also covered by Medicare and Medicaid, though Medicaid benefits vary by state.

Radiation therapy

Radiation therapy is the use of high-energy beams or particles to kill cancer cells and is often used after surgery to destroy cancer cells remaining in the breast, chest wall, or underarm area. BCS is almost always followed by radiation therapy to the breast because it has been shown to reduce the risk of cancer recurrence by about 50% at 10 years and the risk of breast cancer death by almost 20% at 15 years.²¹³ However, radiation is not necessary in women 70 years of age and older with small, lymph node-negative, HR+ cancers, because it hasn't been shown to improve survival in patients who take hormonal therapy for at least five years.²³⁴ Some mastectomy-treated patients also benefit from radiation if their tumor is larger than 5 cm, growing in to nearby tissues, or if cancer is found in the lymph nodes. Radiation can also be used to treat the symptoms of advanced breast cancer, especially when it has spread to the central nervous system or bones.

Radiation therapy may be administered as external beam radiation, brachytherapy, or a combination of both. The method depends on the type, stage, and location of the tumor, as well as patient characteristics, and doctor and patient preference. External beam radiation is the standard type of radiation, whereby radiation from a machine outside the body is focused on the area affected by cancer. Traditionally, external beam radiation therapy

is administered 5 days per week over 5 to 7 weeks, but in select patients a 3-week course appears to be as effective.^{235, 236} Brachytherapy uses a radioactive source placed in catheters or other devices that are put into the cavity left after BCS and is sometimes an option for patients with early-stage breast cancers. Intracavitary brachytherapy is typically given daily for 5 days. Accumulating evidence suggests intracavity brachytherapy may be as effective as whole breast radiation for selected patients, but deliverable in less time and with fewer side effects.²³⁷⁻²⁴⁰ However, most studies of intracavitary brachytherapy have not followed patients for more than 5 years, so its long-term efficacy as compared to whole breast radiation has not been established.

For intraoperative radiation therapy, a single dose of radiation is administered to the tumor bed during breast-conserving surgery. It can be used instead of intracavitary brachytherapy but is only available at limited centers.²⁴¹

Systemic therapy

Systemic therapy is treatment that travels through the bloodstream and affects and treats almost all parts of the body. Systemic therapy includes chemotherapy, hormone therapy, and targeted therapy, all of which work through different mechanisms. For example, chemotherapy drugs generally work by attacking cells that grow quickly, such as cancer cells. Hormone therapy works by either blocking the body's natural hormones or lowering the levels of those hormones, which can act to promote the growth of some cancers. Targeted drugs work by attacking specific molecules in or on cells that may be more common or active in cancer cells.

When systemic treatment is given to patients before surgery, it is called neoadjuvant or preoperative therapy. For larger breast tumors, it is often used to shrink the tumor enough to make surgical removal easier and less extensive (such as BCS in women who would otherwise have required mastectomy). Neoadjuvant systemic therapy has been found to be as effective as the same therapy given after surgery in terms of survival and distant recurrence.²⁴² Systemic treatment given to patients after surgery is called adjuvant therapy. It is used to kill any

undetected tumor cells (micrometastases) that may have migrated to other parts of the body. Systemic therapy is the main treatment option for women with metastatic breast cancer.

Chemotherapy

The benefit of chemotherapy is dependent on multiple factors, including the size of the tumor, the number of lymph nodes involved, the presence of estrogen or progesterone receptors, and the presence of HER2 overexpression on the cancer cells. Triple negative and HER2+ breast cancers tend to be more sensitive to chemotherapy than HR+ tumors.²⁴³ There are also gene expression panels (such as Oncotype DX, PAM 50, and MammaPrint) that can help assess the risk of distant recurrence in women with early-stage, HR+, HER2- breast cancers, and potentially identify those who would more likely benefit from chemotherapy, as well as those who could safely avoid it. The Oncotype Dx 21-Gene Recurrence Score is used most widely in the United States; a high score identifies women who would more likely benefit from adjuvant chemotherapy (in addition to hormone therapy) whereas a low score identifies women who could safely avoid it.²⁴⁴ These scores are independent of patient age and tumor size. Clinical trials are currently underway to further evaluate the predictive value of some of these tests in women with intermediate risk scores and those with node positive disease.

Research has established that combinations of drugs are more effective than one drug alone for treatment of early-stage breast cancer, and several options exist when selecting a chemotherapy regimen. Depending on the combination of drugs used, adjuvant and neoadjuvant chemotherapy is usually given for 3 to 6 months. This treatment is most effective when the full dose and cycle of drugs are completed in a timely manner, without significant delays or interruption.

Hormone (anti-estrogen) therapy

Estrogen, a hormone produced by the ovaries in addition to other tissues, promotes the growth of HR+ breast cancers. Patients with these tumors can be given hormone therapy to lower estrogen levels or block the effects of estrogen on the growth of breast cancer cells.

These drugs are different than menopausal hormone therapies, which actually increase hormone levels. Hormone therapy for breast cancer can be different in premenopausal and postmenopausal women.

Tamoxifen is a treatment that blocks the effects of estrogen in breast tissue but has estrogenic effects in other tissues, such as the liver, uterus, and bones. Tamoxifen can be used to treat both early- and advanced-HR+ breast cancer in both pre- and postmenopausal women. Adjuvant treatment of early-stage HR+ breast cancer with tamoxifen for at least 5 years has been shown to reduce the rate of recurrence by approximately 40%-50% throughout the first decade, and reduces breast cancer mortality by about one-third throughout the first 15 years.²⁴⁵ More recently, studies have shown that extended use of adjuvant tamoxifen (10 years versus 5 years) further reduces the risk of breast cancer recurrence and mortality, so clinical practice guidelines now recommend consideration of adjuvant tamoxifen therapy for 10 years.²⁴⁷

Aromatase inhibitors (AIs), such as letrozole, anastrozole, and exemestane, are another class of drugs used to treat both early- and advanced-HR+ breast cancer. Clinical trials in postmenopausal women have demonstrated a small advantage to including an AI initially or over the course of treatment rather than 5 years of tamoxifen alone.²⁴⁸ Treatment guidelines recommend AIs should usually be included in the treatment of postmenopausal women with HR+ breast cancer.²⁴⁷ Although AIs have fewer serious side effects than tamoxifen, they can cause osteoporosis (with resulting bone fractures), joint pain, and other musculoskeletal symptoms because they completely deplete postmenopausal women of estrogen. Clinical trials continue to assess the optimal timing and duration of these treatments.

The mainstay of treatment for most premenopausal women with HR+ tumors is tamoxifen. Some women may also benefit from surgical removal (oophorectomy) or chemical suppression of the ovaries, which are the main source of estrogen prior to menopause. Potentially reversible ovarian suppression can be achieved with a class of drugs called luteinizing hormone-releasing hormone (LHRH) analogs. Ovarian suppression can also

allow the use of AIs in premenopausal women. Initial results from two ongoing clinical trials comparing premenopausal early-stage breast cancer patients treated with ovarian suppression, plus either an AI or tamoxifen, found greater reduction in risk of recurrence with AIs.²⁴⁹

Adding ovarian suppression to tamoxifen or aromatase inhibitors has been shown to improve survival in premenopausal women with advanced (metastatic) HR+ breast cancer.²⁵⁰ Fulvestrant is another treatment used to treat metastatic breast cancer. It is an anti-estrogen drug given by intramuscular injection that reduces the number of estrogen receptors and blocks estrogen binding.

Targeted therapy

About 17% of breast cancers overproduce the growth-promoting protein HER2/neu, and multiple medications are now approved for the treatment of this subtype.

Trastuzumab, the first approved drug, is a monoclonal antibody that directly targets the HER2 protein. The combined results of two large trials indicate that adding trastuzumab to standard chemotherapy for early-stage HER2+ breast cancer reduces the risk of recurrence and death by 52% and 33%, respectively, compared to chemotherapy alone.²⁵¹ This drug is also a standard part of the treatment for advanced HER2+ breast cancer. Several newer drugs have been developed that target the HER2 protein that can be used in combination with trastuzumab or if trastuzumab is no longer working. All invasive breast cancers should be tested for the HER2 gene amplification or protein overexpression to identify women who would benefit from this therapy.

Other types of targeted therapies can be used along with aromatase inhibitors in women with HR+ breast cancer, where they have been shown to make these hormone therapies more effective.

What Is the American Cancer Society Doing About Breast Cancer?

As an organization of nearly 2 million strong, the American Cancer Society is committed to a world free from the pain and suffering of breast cancer – and all cancers.

Prevention, Early Detection, and Treatment

The American Cancer Society is doing everything in our power to help prevent breast cancer – and all cancers. We promote healthy lifestyles by issuing cancer guidelines for prevention and early detection, helping people avoid tobacco, and reducing barriers to healthy eating and exercise. For those who are diagnosed, we're there every minute of every day.

Information, 24 hours a day, seven days a week

The American Cancer Society is available 24 hours a day, seven days a week online at cancer.org and by calling us at

1-800-227-2345. Callers are connected with caring, trained American Cancer Society staff who can help them locate a hospital, understand breast cancer and treatment options, learn what to expect and how to plan, address insurance concerns, find financial resources, find a local support group, and more. We can also help people who speak languages other than English or Spanish find the assistance they need, offering services in more than 200 languages.

People can visit cancer.org/breastcancer to find information on every aspect of the breast cancer experience, from prevention to survivorship. We also publish a wide variety of pamphlets and books that cover a multitude of topics, from patient education, quality-of-life and caregiving issues to healthy living. Visit cancer.org/bookstore for a complete list of books that are available for order.

Help navigating the health care system

Learning how to navigate the cancer journey and the health care system can be overwhelming for anyone, but it is particularly difficult for those who are medically underserved, those who experience language or health literacy barriers, and those with limited resources. The American Cancer Society Patient Navigator Program reaches those most in need. The largest oncology-focused patient navigator program in the country, it has specially trained patient navigators at more than 120 sites across the nation. Patient navigators can help: find rides to and from cancer-related appointments; assist with medical financial issues, including insurance navigation; identify community resources; and provide information on a patient's cancer diagnosis and treatment process. We collaborate with a variety of organizations, including the National Cancer Institute's Center to Reduce Cancer Health Disparities, the Center for Medicare and Medicaid Services, and numerous cancer treatment centers to implement and evaluate this program.

Breast cancer support

Through the American Cancer Society Reach To Recovery® program, breast cancer patients are paired with trained volunteers who have had similar diagnoses and treatment plans to provide more personal, one-on-one support.

Finding hope and inspiration

Women with breast cancer and their loved ones do not have to face their experience alone. The American Cancer Society Cancer Survivors Network® provides a safe online connection where cancer patients can find others with similar experiences and interests. At csn.cancer.org, members can join chat rooms and build their own support network from among the members.

Transportation to treatment

The American Cancer Society Road To Recovery® program offers cancer patients free transportation to and from their cancer-related treatment. For those who cannot drive themselves or have no other means of getting to treatment, trained volunteers donate their

spare time and the use of their personal vehicle to give cancer patients in their community a much-needed ride. Other transportation programs are also available in certain areas. Call us at 1-800-227-2345 for more information.

Lodging during treatment

The American Cancer Society Hope Lodge® program provides a free home away from home for cancer patients and their caregivers. More than just a roof over their heads, it is a nurturing community where patients can share stories and offer each other emotional support. Through our Hotel Partners Program, we also partner with local hotels across the country to provide free or discounted lodging to patients and their caregivers in communities without a Hope Lodge facility.

Help with appearance-related side effects of treatment

The Look Good Feel Better® program teaches women how to cope with appearance-related side effects of cancer treatment. Group workshops are free and led by licensed volunteer beauty professionals (cosmetologists, estheticians, and nail technicians). Skin care, makeup, and hair loss solution techniques and tips are provided in a supportive environment. Information and materials are also available for men and teens. This program is a collaboration of the American Cancer Society, the Look Good Feel Better Foundation, and the Professional Beauty Association. To learn more, visit the Look Good Feel Better website at lookgoodfeelbetter.org or call 1-800-395-LOOK (1-800-395-5665).

Hair-loss and mastectomy products

Some women wear wigs, hats, breast forms, and special bras to help cope with the effects of a mastectomy and hair loss. The American Cancer Society "tlc" *Tender Loving Care*® publication offers affordable hair loss and mastectomy products, as well as advice on how to use those products. The "tlc"™ products and catalogs may be ordered online at tlcdirect.org or by calling 1-800-850-9445. All proceeds from product sales go back into our survivorship programs and services.

Support after treatment

The end of breast cancer treatment does not mean the end of a cancer journey. Cancer survivors may experience long-term or late effects resulting from the disease or its treatment. The *Life After Treatment: The Next Chapter in Your Survivorship Journey* guide may help cancer survivors as they begin the next phase of their journey. Visit cancer.org/survivorshipguide to download a free copy of the guide.

The American Cancer Society has also recently published a follow-up care guideline for breast cancer survivors that builds upon available evidence, surveillance guidelines, and standard clinical practice and is designed to facilitate the provision of high-quality, standardized, clinical care by primary care providers.²⁵² The breast cancer guideline addresses the assessment and management of potential long-term and late effects, as well as recommendations for health promotion, surveillance for recurrence, screening for second primary cancers, and the coordination of care between specialists and primary care clinicians.

Research

The American Cancer Society invests more in breast cancer research than any other cancer type. Our funded research has led to the development of potentially lifesaving breast cancer drugs such as tamoxifen and Herceptin, as well as improved understanding of genes linked to breast cancer. We are currently funding more than \$59 million in breast cancer research through 159 research and training grants. These grants are awarded in multiple areas relevant to the disease, including genetics, etiology, diagnostics (imaging and biomarkers), drug development; and preclinical, clinical, and epidemiological studies in prevention, diagnosis, treatment, and quality of life.

Specific examples of ongoing breast cancer research being conducted by American Cancer Society grantees include:

- Researching new ways of treating HER2+ breast cancer patients who do not respond to or become resistant to existing targeted therapies

- Evaluating psychosocial interventions aimed at supporting Latinas with breast cancer and their family partners to reduce distress and improve quality of life
- Exploring how a gene called amphiregulin may cause a woman with ER+ breast cancer to become resistant to hormonal therapies
- Investigating ways to prevent breast cancer patients from developing brain metastases by studying proteins that may be involved in the spread of breast cancer to the brain
- Evaluating whether a non-invasive and inexpensive technique called auricular point acupressure can help women with breast cancer manage their pain at home

Internally, the American Cancer Society also conducts epidemiologic studies of breast cancer and performs surveillance research to monitor racial and socioeconomic disparities in breast cancer screening, incidence, survival, and mortality. Using information collected from more than 600,000 women in Cancer Prevention Study-II (CPS-II), American Cancer Society epidemiologists study the influence of many risk factors, including alcohol consumption, diethylstilbestrol (DES), estrogen hormone use, family history of cancer, obesity, smoking, and spontaneous abortion on the risk of death from breast cancer. In order to continue to explore the effects of changing exposures and to provide greater opportunity to integrate biological and genetic factors into studies of other risk factors, more than 304,000 men and women were enrolled in the American Cancer Society Cancer Prevention Study-3 (CPS-3), and nearly all provided a blood sample at the time of enrollment. The blood specimens and questionnaire data collected from CPS-3 participants will provide unique opportunities for research in the US.

Advocacy

The American Cancer Society's nonprofit, nonpartisan advocacy affiliate, the American Cancer Society Cancer Action NetworkSM (ACS CAN), advocates at the federal, state, and local levels to increase access to quality breast

cancer screenings, diagnostic and treatment services, and care for all women; increase government funding for breast cancer research; and provide a voice for the concerns of breast cancer patients and survivors. Following are some of the efforts that ACS CAN has been involved with in the past few years to fight breast cancer – and all cancers:

- **Improving Access to Affordable Care through Health Care Reform:** The Affordable Care Act (ACA) was signed into law on March 23, 2010, giving cancer patients access to quality, affordable health care. All new health insurance plans, including those offered through state health insurance exchanges, are required to cover preventive services rated “A” or “B” by the US Preventive Services Task Force, including mammography screening, at no cost to patients. Additionally, the ACA removed cost sharing for any preventive services covered by Medicare. ACS CAN advocates for clear, comprehensive coverage of these preventive services, including breast cancer screening, and encourages states to broaden access to health care coverage for all low-income Americans through state Medicaid programs.
- **The National Breast and Cervical Cancer Early Detection Program (NBCCEDP):** Protecting and increasing funding for the NBCCEDP is a high priority for ACS CAN at both the state and federal levels. Administered by the Centers for Disease Control and Prevention, this successful program provides community-based breast and cervical cancer screenings to low-income, uninsured, and underinsured women. More than 50% of the women screened are from racial/ethnic minority groups. Currently, only one in 10 eligible women can be served by the program due to federal funding cuts. ACS CAN is asking Congress to increase funding to ensure that more women have access to cancer screening.
- **Protecting the Breast and Cervical Cancer Prevention and Treatment Act (BCCPTA):** In 2000, Congress passed the BCCPTA, ensuring that low-income women diagnosed with cancer through the NBCCEDP were provided a pathway to treatment services through their state Medicaid program.

In recent years, a number of states have considered proposals to eliminate the treatment program due to misconceptions around coverage needs following implementation of the ACA.

- **The Breast Density and Mammography Reporting Act:** Mammography sensitivity is lower for women with mammographically dense breasts because dense breast tissue makes it harder for doctors to see cancer on mammograms. The federal Breast Density and Mammography Reporting Act directs an evidence-based process to inform women about breast density and risk. Additionally, this legislation encourages new research to support the creation of clinical guidelines and best practices for screening of and reports to women with mammographically dense breasts.
- **Patient Navigation:** Patient navigation can improve quality of cancer care, particularly in vulnerable populations. ACS CAN supports the federal Patient Navigation Assistance Act, which would create a coverage solution that incentivizes providers to use patient navigators in order to improve care coordination for patients. The organization also is working with Congress and federal agencies to help increase funding for patient navigation programs.
- **Funding for Cancer Research:** ACS CAN continues to work to increase government funding for cancer research at the National Institutes of Health, including the National Cancer Institute and the National Center on Minority Health and Health Disparities.

It is important to note that the preceding references to ACA provisions and other federal laws and guidance reflect current law as of July 18, 2017, and do not take into account potential changes to the ACA or other federal laws and guidance subsequently considered by Congress and the administration.

Sources of Statistics

General information. Unless otherwise stated, the statistics and statements in this booklet refer to invasive (not *in situ*) female breast cancer.

Estimated new breast cancer cases. The overall estimated number of new *in situ* and invasive breast cancer cases diagnosed in the US in 2017 was projected using a spatiotemporal model based on incidence data from 49 states and the District of Columbia for the years 1995-2013 that met the North American Association of Central Cancer Registries' (NAACCR) high-quality data standard for incidence. This method considers geographic variations in sociodemographic and lifestyle factors, medical settings, and cancer screening behaviors as predictors of incidence, and also accounts for expected delays in case reporting. Estimates for specific age groups are based on the proportions of cases diagnosed in each age group in the NAACCR data during 2010-2014 applied to the overall 2017 estimate.

Incidence rates. Incidence rates are defined as the number of people per 100,000 who develop a disease during a given time period. All incidence rates in this publication are age adjusted to the 2000 US standard population to allow comparisons across populations with different age distributions. Breast cancer incidence rates for the US in the most recent time period were calculated using data on cancer cases collected by NAACCR and population data collected by the US Census Bureau. When referenced as such, NAACCR incidence data were made available on the NAACCR website (naaccr.org) and within the Cancer in North America publications.^{253,254} Long-term incidence trends are based on American Cancer Society analysis of the SEER 9 Registries Public Use Dataset using SEER*Stat 8.3.4, a statistical software package from the National Cancer Institute.^{255,256} Short-term trends by race/ethnicity, age, tumor size, and stage at diagnosis are based on delay-adjusted incidence rates from the SEER 13 registries.²² When referenced as such, US SEER incidence rates and trends were previously made available on SEER's website (seer.cancer.gov) and within the *SEER Cancer Statistics Review 1975-2014*.¹⁷

Note that because of delays in reporting newly diagnosed cancer cases to the cancer registries, cancer incidence rates for the most recent diagnosis years may be underestimated. Incidence rates adjusted for delays in reporting are used when available and are referenced as such.

Estimated breast cancer deaths. The overall estimated number of breast cancer deaths in the US is calculated by fitting the number of breast cancer deaths for 1997-2014 to a statistical model that forecasts the number of deaths expected to occur in 2017. Data on the number of deaths are obtained from the National Center for Health Statistics (NCHS) at the Centers for Disease Control and Prevention. Age-specific estimates were calculated using the proportions of deaths that occurred in each age group during 2011-2015 applied to the overall 2017 estimate.

Mortality rates. Similar to incidence rates, mortality rates are defined as the number of people per 100,000 who die from a disease during a given time period. Death rates used in this publication were previously made available by SEER on their website (seer.cancer.gov) and within the *SEER Cancer Statistics Review 1975-2014*.¹⁷ Death rates were calculated using data on cancer deaths compiled by NCHS and population data collected by the US Census Bureau. All death rates in this publication were age adjusted to the 2000 US standard population.

Survival. Five-year survival statistics are based on cancer patients diagnosed during 2007-2013; 10-year survival rates are based on diagnoses during 2001-2013; and 15-year survival rates are based on diagnoses during 1996-2013. All patients were followed through 2014. Relative survival rates are used to adjust for normal life expectancy (and events such as death from heart disease, accidents, and diseases of old age). Relative survival is calculated by dividing the percentage of observed 5-year survival for cancer patients by the 5-year survival expected for people in the general population who are similar to the patient group with respect to age, sex, race, and calendar year of observation. Cause-specific survival rates are the probability of not dying of breast cancer

within 5 years after diagnosis. When referenced as such, 5-year survival statistics were originally published in *SEER Cancer Statistics Review, 1975-2014*.¹⁷

Probability of developing cancer. Probabilities of developing breast cancer were calculated using DevCan 6.7.5 (Probability of Developing Cancer Software), developed by the National Cancer Institute.²⁵⁷ These probabilities reflect the average experience of women in the US and do not take into account individual behaviors and risk factors (e.g., utilization of mammography screening and family history of breast cancer).

Screening. Prevalence estimates of mammography by age and state were obtained through analysis of data from the Behavioral Risk Factor Surveillance System (BRFSS).¹⁹⁶ The BRFSS is an ongoing system of surveys conducted by the state health departments in cooperation with the Centers for Disease Control and

Prevention. Prevalence estimates of mammography by race/ethnicity, poverty, and other demographic factors are from the National Health Interview Survey.¹⁹⁵

Important note about estimated cases and deaths. The estimated numbers of new breast cancer cases and deaths in 2017 should be interpreted with caution. The projection method is model-based, so the estimated numbers may vary from previous years for reasons other than changes in cancer occurrence. Therefore, while 3-year-ahead projections provide a reasonably accurate estimate of the cancer burden in 2017, we strongly discourage the use of our estimates to track changes in cancer occurrence. Age-adjusted incidence and mortality rates reported by the SEER program and the NCHS, respectively, are the preferred statistics to track cancer trends in the US. Rates from state cancer registries are useful for tracking local trends.

References

1. Edge SB, Byrd DR, Compton CC, Fritz AG, Greene FG, Trotti A. *AJCC Cancer Staging Manual*. New York: Springer, 2010.
2. Giuliano AE, Connolly JL, Edge SB, et al. Breast Cancer – Major changes in the American Joint Committee on Cancer eighth edition cancer staging manual. *CA Cancer J Clin*. 2017;67: 290-303.
3. Allred DC. Ductal carcinoma in situ: terminology, classification, and natural history. *J Natl Cancer Inst Monogr*. 2010;2010: 134-138.
4. Erbas B, Provenzano E, Armes J, Gertig D. The natural history of ductal carcinoma in situ of the breast: a review. *Breast Cancer Res Treat*. 2006;97: 135-144.
5. Sanders ME, Schuyler PA, Dupont WD, Page DL. The natural history of low-grade ductal carcinoma in situ of the breast in women treated by biopsy only revealed over 30 years of long-term follow-up. *Cancer*. 2005;103: 2481-2484.
6. Collins LC, Tamimi RM, Baer HJ, Connolly JL, Colditz GA, Schnitt SJ. Outcome of patients with ductal carcinoma in situ untreated after diagnostic biopsy: results from the Nurses' Health Study. *Cancer*. 2005;103: 1778-1784.
7. Eusebi V, Feudale E, Foschini MP, et al. Long-term follow-up of in situ carcinoma of the breast. *Seminars in Diagn Path*. 1994;11: 223-235.
8. Dieci MV, Orvieto E, Dominici M, Conte P, Guarneri V. Rare breast cancer subtypes: histological, molecular, and clinical peculiarities. *Oncologist*. 2014;19: 805-813.
9. Tamimi RM, Colditz GA, Hazra A, et al. Traditional breast cancer risk factors in relation to molecular subtypes of breast cancer. *Breast Cancer Res Treat*. 2012;131: 159-167.
10. Cancer Genome Atlas Network. Comprehensive molecular portraits of human breast tumours. *Nature*. 2012;490: 61-70.
11. Cheang MC, Martin M, Nielsen TO, et al. Defining breast cancer intrinsic subtypes by quantitative receptor expression. *Oncologist*. 2015;20: 474-482.
12. Blows FM, Driver KE, Schmidt MK, et al. Subtyping of breast cancer by immunohistochemistry to investigate a relationship between subtype and short and long term survival: a collaborative analysis of data for 10,159 cases from 12 studies. *PLoS Med*. 2010;7: e1000279.
13. Haque R, Ahmed SA, Inzhakova G, et al. Impact of breast cancer subtypes and treatment on survival: an analysis spanning two decades. *Cancer Epidemiol Biomarkers Prev*. 2012;21: 1848-1855.
14. Perou CM, Borresen-Dale AL. Systems biology and genomics of breast cancer. *Cold Spring Harb Perspect Biol*. 2011;3.
15. Bianchini G, Balko JM, Mayer IA, Sanders ME, Gianni L. Triple-negative breast cancer: challenges and opportunities of a heterogeneous disease. *Nature Rev Clin Oncol*. 2016;13: 674-690.
16. Miller KD, Siegel RL, Lin CC, et al. Cancer treatment and survivorship statistics, 2016. *CA Cancer J Clin*. 2016;66: 271-289.
17. Howlader N, Noone AM, Krapcho M, et al. *SEER Cancer Statistics Review, 1975-2014*. https://seer.cancer.gov/csr/1975_2014/, based on November 2016 SEER data submission, posted to the SEER web site, April 2017. Bethesda, MD: National Cancer Institute, 2017.
18. White MC, Espy DK, Swan J, Wiggins CL, Eheman C, Kaur JS. Disparities in cancer mortality and incidence among American Indians and Alaska Natives in the United States. *Amer J Pub Health*. 2014;104 Suppl 3: S377-387.

19. Ravdin PM, Cronin KA, Howlader N, et al. The decrease in breast cancer incidence in 2003 in the United States. *N Engl J Med.* 2007;356: 1670-1674.
20. Coombs NJ, Cronin KA, Taylor RJ, Freedman AN, Boyages J. The impact of changes in hormone therapy on breast cancer incidence in the US population. *Cancer Causes Control.* 2010;21: 83-90.
21. DeSantis C, Howlader N, Cronin KA, Jemal A. Breast cancer incidence rates in U.S. women are no longer declining. *Cancer Epidemiol Biomarkers Prev.* 2011;20: 733-739.
22. Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database: Incidence – SEER 13 Regs Research Data with Delay-Adjustment, Malignant Only, Nov 2016 Sub (1992-2014) <Katrina/Rita Population Adjustment> – Linked To County Attributes – Total U.S., 1969-2015 Counties, National Cancer Institute, DCCPS, Surveillance Research Program, released April 2017, based on the November 2016 submission.
23. Berry DA, Cronin KA, Plevritis SK, et al. Effect of screening and adjuvant therapy on mortality from breast cancer. *N Engl J Med.* 2005;353: 1784-1792.
24. Newman LA, Kaljee LM. Health Disparities and Triple-Negative Breast Cancer in African American Women: A Review. *JAMA Surg.* 2017.
25. Roberts MC, Wheeler SB, Reeder-Hayes K. Racial/Ethnic and socioeconomic disparities in endocrine therapy adherence in breast cancer: a systematic review. *Amer J Public Health.* 2015;105 Suppl 3: e4-e15.
26. Iqbal J, Ginsburg O, Rochon PA, Sun P, Narod SA. Differences in breast cancer stage at diagnosis and cancer-specific survival by race and ethnicity in the United States. *JAMA.* 2015;313: 165-173.
27. Daly B, Olopade OI. A perfect storm: How tumor biology, genomics, and health care delivery patterns collide to create a racial survival disparity in breast cancer and proposed interventions for change. *CA Cancer J Clin.* 2015;65: 221-238.
28. Allgood KL, Rauscher GH, Whitman S, Vasquez-Jones G, Shah AM. Validating self-reported mammography use in vulnerable communities: findings and recommendations. *Cancer Epidemiol Biomarkers Prev.* 2014;23: 1649-1658.
29. Njai R, Siegel PZ, Miller JW, Liao Y. Misclassification of survey responses and black-white disparity in mammography use, Behavioral Risk Factor Surveillance System, 1995-2006. *Prev Chronic Dis.* 2011;8: A59.
30. Cronin KA, Miglioretti DL, Krapcho M, et al. Bias associated with self-report of prior screening mammography. *Cancer Epidemiol Biomarkers Prev.* 2009;18: 1699-1705.
31. Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database: Incidence – SEER 18 Regs Research Data, Nov 2016 Sub (2000-2014) <Katrina/Rita Population Adjustment> – Linked To County Attributes – Total U.S., 1969-2015 Counties, National Cancer Institute, DCCPS, Surveillance Research Program, released April 2017, based on the November 2016 submission.
32. Keegan TH, Kurian AW, Gali K, et al. Racial/ethnic and socioeconomic differences in short-term breast cancer survival among women in an integrated health system. *Amer J Public Health.* 2015;105: 938-946.
33. Shariff-Marco S, Yang J, John EM, et al. Impact of neighborhood and individual socioeconomic status on survival after breast cancer varies by race/ethnicity: the Neighborhood and Breast Cancer Study. *Cancer Epidemiol Biomarkers Prev.* 2014;23: 793-811.
34. Shi R, Taylor H, McLarty J, Liu L, Mills G, Burton G. Effects of payer status on breast cancer survival: a retrospective study. *BMC Cancer.* 2015;15: 211.
35. Kish JK, Yu M, Percy-Laury A, Altekuruse SF. Racial and ethnic disparities in cancer survival by neighborhood socioeconomic status in Surveillance, Epidemiology, and End Results (SEER) Registries. *J Natl Cancer Inst Monogr.* 2014;2014: 236-243.
36. Sprague BL, Trentham-Dietz A, Gangnon RE, et al. Socioeconomic status and survival after an invasive breast cancer diagnosis. *Cancer.* 2011;117: 1542-1551.
37. Anderson WF, Jatoi I, Tse J, Rosenberg PS. Male breast cancer: a population-based comparison with female breast cancer. *J Clin Oncol.* 2010;28: 232-239.
38. Brinton LA, Cook MB, McCormack V, et al. Anthropometric and hormonal risk factors for male breast cancer: male breast cancer pooling project results. *J Natl Cancer Inst.* 2014;106: djt465.
39. Ruddy KJ, Winer EP. Male breast cancer: risk factors, biology, diagnosis, treatment, and survivorship. *Ann Oncol.* 2013;24: 1434-1443.
40. Tamimi RM, Spiegelman D, Smith-Warner SA, et al. Population Attributable Risk of Modifiable and Nonmodifiable Breast Cancer Risk Factors in Postmenopausal Breast Cancer. *Am J Epidemiol.* 2016;184: 884-893.
41. Liu Y, Nguyen N, Colditz GA. Links between alcohol consumption and breast cancer: a look at the evidence. *Women's Health* (London, England). 2015;11: 65-77.
42. Dall GV, Britt KL. Estrogen Effects on the Mammary Gland in Early and Late Life and Breast Cancer Risk. *Front Oncol.* 2017;7: 110.
43. Barnard ME, Boeke CE, Tamimi RM. Established breast cancer risk factors and risk of intrinsic tumor subtypes. *Biochim Biophys Acta.* 2015;1856: 73-85.
44. Collaborative Group on Hormonal Factors in Breast Cancer. Familial breast cancer: collaborative reanalysis of individual data from 52 epidemiological studies including 58,209 women with breast cancer and 101,986 women without the disease. *Lancet.* 2001;358: 1389-1399.
45. Turnbull C, Rahman N. Genetic predisposition to breast cancer: past, present, and future. *Ann Rev Genomics Hum Genet.* 2008;9: 321-345.
46. Tung N, Lin NU, Kidd J, et al. Frequency of Germline Mutations in 25 Cancer Susceptibility Genes in a Sequential Series of Patients With Breast Cancer. *J Clin Oncol.* 2016;34: 1460-1468.
47. Gabai-Kapara E, Lahad A, Kaufman B, et al. Population-based screening for breast and ovarian cancer risk due to BRCA1 and BRCA2. *Proc Natl Acad Sci U S A.* 2014;111: 14205-14210.
48. Kuchenbaecker KB, Hopper JL, Barnes DR, et al. Risks of Breast, Ovarian, and Contralateral Breast Cancer for BRCA1 and BRCA2 Mutation Carriers. *JAMA.* 2017;317: 2402-2416.
49. Antoniou AC, Casadei S, Heikkinen T, et al. Breast-cancer risk in families with mutations in PALB2. *N Engl J Med.* 2014;371: 497-506.
50. Michailidou K, Beesley J, Lindstrom S, et al. Genome-wide association analysis of more than 120,000 individuals identifies 15 new susceptibility loci for breast cancer. *Nature Genetics.* 2015;47: 373-380.
51. Lichtenstein P, Holm NV, Verkasalo PK, et al. Environmental and heritable factors in the causation of cancer – analyses of cohorts of twins from Sweden, Denmark, and Finland. *N Engl J Med.* 2000;343: 78-85.

52. Moyer VA. Risk assessment, genetic counseling, and genetic testing for BRCA-related cancer in women: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med.* 2014;160: 271-281.
53. Nichols HB, Berrington de Gonzalez A, Lacey JV, Jr., Rosenberg PS, Anderson WF. Declining incidence of contralateral breast cancer in the United States from 1975 to 2006. *J Clin Oncol.* 2011;29: 1564-1569.
54. Gierach GL, Curtis RE, Pfeiffer RM, et al. Association of Adjuvant Tamoxifen and Aromatase Inhibitor Therapy With Contralateral Breast Cancer Risk Among US Women With Breast Cancer in a General Community Setting. *JAMA Oncol.* 2016.
55. Lopez-Garcia MA, Geyer FC, Lacroix-Triki M, Marchio C, Reis-Filho JS. Breast cancer precursors revisited: molecular features and progression pathways. *Histopathology.* 2010;57: 171-192.
56. Morrow M, Schnitt SJ, Norton L. Current management of lesions associated with an increased risk of breast cancer. *Nat Rev Clin Oncol.* 2015;12: 227-238.
57. King TA, Pilewskie M, Muhsen S, et al. Lobular Carcinoma in Situ: A 29-Year Longitudinal Experience Evaluating Clinicopathologic Features and Breast Cancer Risk. *J Clin Oncol.* 2015;33: 3945-3952.
58. Dyrstad SW, Yan Y, Fowler AM, Colditz GA. Breast cancer risk associated with benign breast disease: systematic review and meta-analysis. *Breast Cancer Res Treat.* 2015;149: 569-575.
59. Bertrand KA, Scott CG, Tamimi RM, et al. Dense and nondense mammographic area and risk of breast cancer by age and tumor characteristics. *Cancer Epidemiol Biomarkers Prev.* 2015;24: 798-809.
60. Sprague BL, Gangnon RE, Burt V, et al. Prevalence of mammographically dense breasts in the United States. *J Natl Cancer Inst.* 2014;106.
61. Boyd NF, Martin LJ, Rommens JM, et al. Mammographic density: a heritable risk factor for breast cancer. *Methods Mol Biol.* 2009;472: 343-360.
62. Harris HR, Tamimi RM, Willett WC, Hankinson SE, Michels KB. Body size across the life course, mammographic density, and risk of breast cancer. *Am J Epidemiol.* 2011;174: 909-918.
63. Boyd NF. Tamoxifen, mammographic density, and breast cancer prevention. *J Natl Cancer Inst.* 2011;103: 704-705.
64. Byrne C, Ursin G, Martin CF, et al. Mammographic Density Change With Estrogen and Progestin Therapy and Breast Cancer Risk. *J Natl Cancer Inst.* 2017;109.
65. Boyd NF, Guo H, Martin LJ, et al. Mammographic density and the risk and detection of breast cancer. *N Engl J Med.* 2007;356: 227-236.
66. DenseBreast-Info, Inc. LEGISLATION AND REGULATIONS – WHAT IS REQUIRED? Available from URL: densebreast-info.org/legislation Accessed August 22, 2017.
67. Melnikow J, Fenton JJ, Whitlock EP, et al. Supplemental Screening for Breast Cancer in Women with Dense Breasts: A Systematic Review for the U.S. Preventive Services Task Force 2016. *Ann Intern Med.* 2016;164: 268-278.
68. Trubo R. Recent findings may inform breast density notification laws. *JAMA.* 2015;313: 452-453.
69. van den Brandt PA, Spiegelman D, Yaun SS, et al. Pooled analysis of prospective cohort studies on height, weight, and breast cancer risk. *Am J Epidemiol.* 2000;152: 514-527.
70. Green J, Cairns BJ, Casabonne D, Wright FL, Reeves G, Beral V. Height and cancer incidence in the Million Women Study: prospective cohort, and meta-analysis of prospective studies of height and total cancer risk. *Lancet Oncol.* 2011;12: 785-794.
71. WIREN S, HAGGSTROM C, ULMER H, et al. Pooled cohort study on height and risk of cancer and cancer death. *Cancer Causes Control.* 2014;25: 151-159.
72. Collaborative Group on Hormonal Factors in Breast Cancer. Menarche, menopause, and breast cancer risk: individual participant meta-analysis, including 118,964 women with breast cancer from 117 epidemiological studies. *Lancet Oncol.* 2012;13: 1141-1151.
73. Anderson KN, Schwab RB, Martinez ME. Reproductive risk factors and breast cancer subtypes: a review of the literature. *Breast Cancer Res Treat.* 2014;144: 1-10.
74. Qu X, Zhang X, Qin A, et al. Bone mineral density and risk of breast cancer in postmenopausal women. *Breast Cancer Res Treat.* 2013;138: 261-271.
75. Grenier D, Cooke AL, Lix L, Metge C, Lu H, Leslie WD. Bone mineral density and risk of postmenopausal breast cancer. *Breast Cancer Res Treat.* 2011;126: 679-686.
76. Kerlikowske K, Shepherd J, Creasman J, Tice JA, Ziv E, Cummings SR. Are breast density and bone mineral density independent risk factors for breast cancer? *J Natl Cancer Inst.* 2005;97: 368-374.
77. Sampson JN, Falk RT, Schairer C, et al. Association of Estrogen Metabolism with Breast Cancer Risk in Different Cohorts of Postmenopausal Women. *Cancer Res.* 2017;77: 918-925.
78. Endogenous Hormones Breast Cancer Collaborative Group, Key TJ, Appleby PN, et al. Circulating sex hormones and breast cancer risk factors in postmenopausal women: reanalysis of 13 studies. *Br J Cancer.* 2011;105: 709-722.
79. Key TJ, Appleby PN, Reeves GK, et al. Sex hormones and risk of breast cancer in premenopausal women: a collaborative reanalysis of individual participant data from seven prospective studies. *Lancet Oncol.* 2013;14: 1009-1019.
80. Lambertini M, Santoro L, Del Mastro L, et al. Reproductive behaviors and risk of developing breast cancer according to tumor subtype: A systematic review and meta-analysis of epidemiological studies. *Cancer Treat Rev.* 2016;49: 65-76.
81. Albrektsen G, Heuch I, Hansen S, Kvale G. Breast cancer risk by age at birth, time since birth and time intervals between births: exploring interaction effects. *Br J Cancer.* 2005;92: 167-175.
82. Schedin P. Pregnancy-associated breast cancer and metastasis. *Nature Rev Cancer.* 2006;6: 281-291.
83. Brinton LA. Fertility Status and Cancer. *Semin Reprod Med.* 2017;35: 291-297.
84. Brinton LA, Scoccia B, Moghissi KS, et al. Long-term relationship of ovulation-stimulating drugs to breast cancer risk. *Cancer Epidemiol Biomarkers Prev.* 2014;23: 584-593.
85. van den Belt-Dusebout AW, Spaan M, Lambalk CB, et al. Ovarian Stimulation for In Vitro Fertilization and Long-term Risk of Breast Cancer. *JAMA.* 2016;316: 300-312.
86. Faupel-Badger JM, Arcaro KF, Balkam JJ, et al. Postpartum remodeling, lactation, and breast cancer risk: summary of a National Cancer Institute-sponsored workshop. *J Natl Cancer Inst.* 2013;105: 166-174.
87. Collaborative Group on Hormonal Factors in Breast Cancer. Breast cancer and breastfeeding: collaborative reanalysis of individual data from 47 epidemiological studies in 30 countries, including 50,302 women with breast cancer and 96,973 women without the disease. *Lancet.* 2002;360: 187-195.
88. Britt K, Ashworth A, Smalley M. Pregnancy and the risk of breast cancer. *Endocrine-related Cancer.* 2007;14: 907-933.

89. Sisti JS, Collins LC, Beck AH, Tamimi RM, Rosner BA, Eliassen AH. Reproductive risk factors in relation to molecular subtypes of breast cancer: Results from the nurses' health studies. *Int J Cancer*. 2016;138: 2346-2356.
90. Islami F, Liu Y, Jemal A, et al. Breastfeeding and breast cancer risk by receptor status – a systematic review and meta-analysis. *Ann Oncol*. 2015;26: 2398-2407.
91. Bassuk SS, Manson JE. Oral contraceptives and menopausal hormone therapy: relative and attributable risks of cardiovascular disease, cancer, and other health outcomes. *Ann Epidemiol*. 2015;25: 193-200.
92. Li CI, Beaber EF, Tang MT, Porter PL, Daling JR, Malone KE. Effect of depo-medroxyprogesterone acetate on breast cancer risk among women 20 to 44 years of age. *Cancer Res*. 2012;72: 2028-2035.
93. Shantakumar S, Terry MB, Paykin A, et al. Age and menopausal effects of hormonal birth control and hormone replacement therapy in relation to breast cancer risk. *Am J Epidemiol*. 2007;165: 1187-1198.
94. Strom BL, Berlin JA, Weber AL, et al. Absence of an effect of injectable and implantable progestin-only contraceptives on subsequent risk of breast cancer. *Contraception*. 2004;69: 353-360.
95. Ellingjord-Dale M, Vos L, Tretli S, Hofvind S, Dos-Santos-Silva I, Ursin G. Parity, hormones and breast cancer subtypes – results from a large nested case-control study in a national screening program. *Breast Cancer Res*. 2017;19: 10.
96. Soini T, Hurskainen R, Grenman S, Maenpaa J, Paavonen J, Pukkala E. Cancer risk in women using the levonorgestrel-releasing intrauterine system in Finland. *Obstet Gynecol*. 2014;124: 292-299.
97. Dinger J, Bardenheuer K, Minh TD. Levonorgestrel-releasing and copper intrauterine devices and the risk of breast cancer. *Contraception*. 2011;83: 211-217.
98. Trinh XB, Tjalma WA, Makar AP, Buytaert G, Weyler J, van Dam PA. Use of the levonorgestrel-releasing intrauterine system in breast cancer patients. *Fertil Steril*. 2008;90: 17-22.
99. Chlebowski RT, Manson JE, Anderson GL, et al. Estrogen plus progestin and breast cancer incidence and mortality in the Women's Health Initiative Observational Study. *J Natl Cancer Inst*. 2013;105: 526-535.
100. Manson JE, Chlebowski RT, Stefanick ML, et al. Menopausal hormone therapy and health outcomes during the intervention and extended poststopping phases of the Women's Health Initiative randomized trials. *JAMA*. 2013;310: 1353-1368.
101. Beral V, Reeves G, Bull D, Green J. Breast cancer risk in relation to the interval between menopause and starting hormone therapy. *J Natl Cancer Inst*. 2011;103: 296-305.
102. Chlebowski RT, Rohan TE, Manson JE, et al. Breast Cancer After Use of Estrogen Plus Progestin and Estrogen Alone: Analyses of Data From 2 Women's Health Initiative Randomized Clinical Trials. *JAMA Oncol*. 2015;1: 296-305.
103. LaCroix AZ, Chlebowski RT, Manson JE, et al. Health outcomes after stopping conjugated equine estrogens among postmenopausal women with prior hysterectomy: a randomized controlled trial. *JAMA*. 2011;305: 1305-1314.
104. Nelson HD, Walker M, Zakher B, Mitchell J. Menopausal hormone therapy for the primary prevention of chronic conditions: a systematic review to update the U.S. Preventive Services Task Force recommendations. *Ann Intern Med*. 2012;157: 104-113.
105. Calle EE, Feigelson HS, Hildebrand JS, Teras LR, Thun MJ, Rodriguez C. Postmenopausal hormone use and breast cancer associations differ by hormone regimen and histologic subtype. *Cancer*. 2009;115: 936-945.
106. Bakken K, Fournier A, Lund E, et al. Menopausal hormone therapy and breast cancer risk: impact of different treatments. The European Prospective Investigation into Cancer and Nutrition. *Int J Cancer*. 2011;128: 144-156.
107. Chlebowski RT, Anderson GL. The influence of time from menopause and mammography on hormone therapy-related breast cancer risk assessment. *J Natl Cancer Inst*. 2011;103: 284-285.
108. La Vecchia C, Giordano SH, Hortobagyi GN, Chabner B. Overweight, obesity, diabetes, and risk of breast cancer: interlocking pieces of the puzzle. *Oncologist*. 2011;16: 726-729.
109. Gunter MJ, Wang T, Cushman M, et al. Circulating Adipokines and Inflammatory Markers and Postmenopausal Breast Cancer Risk. *J Natl Cancer Inst*. 2015;107.
110. Picon-Ruiz M, Morata-Tarifa C, Friedman ER, Singerland JM. Obesity and adverse breast cancer risk and outcome: mechanistic insights and strategies for intervention. *CA Cancer J Clin*. 2017.
111. Tsilidis KK, Kasimis JC, Lopez DS, Ntzani EE, Ioannidis JP. Type 2 diabetes and cancer: umbrella review of meta-analyses of observational studies. *BMJ*. 2015;350: g7607.
112. Maskarinec G, Jacobs S, Park SY, et al. Type II Diabetes, Obesity, and Breast Cancer Risk: The Multiethnic Cohort. *Cancer Epidemiol Biomarkers Prev*. 2017;26: 854-861.
113. Boyle P, Boniol M, Koechlin A, et al. Diabetes and breast cancer risk: a meta-analysis. *Br J Cancer*. 2012;107: 1608-1617.
114. Keum N, Greenwood DC, Lee DH, et al. Adult weight gain and adiposity-related cancers: a dose-response meta-analysis of prospective observational studies. *J Natl Cancer Inst*. 2015;107.
115. Emaus MJ, van Gils CH, Bakker MF, et al. Weight change in middle adulthood and breast cancer risk in the EPIC-PANACEA study. *Int J Cancer*. 2014;135: 2887-2899.
116. Eliassen AH, Colditz GA, Rosner B, Willett WC, Hankinson SE. Adult weight change and risk of postmenopausal breast cancer. *JAMA*. 2006;296: 193-201.
117. Teras LR, Goodman M, Patel AV, Diver WR, Flanders WD, Feigelson HS. Weight loss and postmenopausal breast cancer in a prospective cohort of overweight and obese US women. *Cancer Causes Control*. 2011;22: 573-579.
118. Nelson HD, Zakher B, Cantor A, et al. Risk factors for breast cancer for women aged 40 to 49 years: a systematic review and meta-analysis. *Ann Intern Med*. 2012;156: 635-648.
119. Pizot C, Boniol M, Mullie P, et al. Physical activity, hormone replacement therapy and breast cancer risk: A meta-analysis of prospective studies. *Eur J Cancer*. 2016;52: 138-154.
120. Hildebrand JS, Gapstur SM, Campbell PT, Gaudet MM, Patel AV. Recreational physical activity and leisure-time sitting in relation to postmenopausal breast cancer risk. *Cancer Epidemiol Biomarkers Prev*. 2013;22: 1906-1912.
121. Neilson HK, Friedenreich CM, Brockton NT, Millikan RC. Physical activity and postmenopausal breast cancer: proposed biologic mechanisms and areas for future research. *Cancer Epidemiol Biomarkers Prev*. 2009;18: 11-27.
122. Cao Y, Hou L, Wang W. Dietary total fat and fatty acids intake, serum fatty acids and risk of breast cancer: A meta-analysis of prospective cohort studies. *Int J Cancer*. 2016;138: 1894-1904.

123. Chen M, Rao Y, Zheng Y, et al. Association between soy isoflavone intake and breast cancer risk for pre- and post-menopausal women: a meta-analysis of epidemiological studies. *PloS one*. 2014;9: e89288.
124. Farvid MS, Chen WY, Michels KB, Cho E, Willett WC, Eliassen AH. Fruit and vegetable consumption in adolescence and early adulthood and risk of breast cancer: population based cohort study. *BMJ*. 2016;353: i2343.
125. Emaus MJ, Peeters PH, Bakker MF, et al. Vegetable and fruit consumption and the risk of hormone receptor-defined breast cancer in the EPIC cohort. *Am J Clin Nutr*. 2016;103: 168-177.
126. Jung S, Spiegelman D, Baglietto L, et al. Fruit and vegetable intake and risk of breast cancer by hormone receptor status. *J Natl Cancer Inst*. 2013;105: 219-236.
127. Bakker MF, Peeters PH, Klaasen VM, et al. Plasma carotenoids, vitamin C, tocopherols, and retinol and the risk of breast cancer in the European Prospective Investigation into Cancer and Nutrition cohort. *Am J Clin Nutr*. 2016;103: 454-464.
128. Eliassen AH, Liao X, Rosner B, Tamimi RM, Tworoger SS, Hankinson SE. Plasma carotenoids and risk of breast cancer over 20 y of follow-up. *Am J Clin Nutr*. 2015;101: 1197-1205.
129. Wang Y, Gapstur SM, Gaudet MM, Furtado JD, Campos H, McCullough ML. Plasma carotenoids and breast cancer risk in the Cancer Prevention Study II Nutrition Cohort. *Cancer Causes Control*. 2015.
130. Jayasekara H, MacInnis RJ, Hodge AM, et al. Is breast cancer risk associated with alcohol intake before first full-term pregnancy? *Cancer Causes Control*. 2016;27: 1167-1174.
131. Singletary KW, Gapstur SM. Alcohol and breast cancer: review of epidemiologic and experimental evidence and potential mechanisms. *JAMA*. 2001;286: 2143-2151.
132. Jung S, Wang M, Anderson K, et al. Alcohol consumption and breast cancer risk by estrogen receptor status: in a pooled analysis of 20 studies. *Int J Epidemiol*. 2016;45: 916-928.
133. Macacu A, Autier P, Boniol M, Boyle P. Active and passive smoking and risk of breast cancer: a meta-analysis. *Breast Cancer Res Treat*. 2015;154: 213-224.
134. Dossus L, Boutron-Ruault MC, Kaaks R, et al. Active and passive cigarette smoking and breast cancer risk: results from the EPIC cohort. *Int J Cancer*. 2014;134: 1871-1888.
135. Gaudet MM, Gapstur SM, Sun J, Diver WR, Hannan LM, Thun MJ. Active smoking and breast cancer risk: original cohort data and meta-analysis. *J Natl Cancer Inst*. 2013;105: 515-525.
136. White AJ, D'Aloisio AA, Nichols HB, DeRoo LA, Sandler DP. Breast cancer and exposure to tobacco smoke during potential windows of susceptibility. *Cancer Causes Control*. 2017;28: 667-675.
137. US Department of Health and Human Services. *The Health Consequences of Smoking – 50 Years of Progress. A Report of the Surgeon General*. Atlanta, GA: US Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, 2014. Printed with corrections, January 2014.
138. Preston DL, Mattsson A, Holmberg E, Shore R, Hildreth NG, Boice JD, Jr. Radiation effects on breast cancer risk: a pooled analysis of eight cohorts. *Radiat Res*. 2002;158: 220-235.
139. Travis LB, Hill DA, Dores GM, et al. Breast cancer following radiotherapy and chemotherapy among young women with Hodgkin disease. *JAMA*. 2003;290: 465-475.
140. Russo J, Hu YF, Yang X, Russo IH. Developmental, cellular, and molecular basis of human breast cancer. *J Natl Cancer Inst Monogr*. 2000: 17-37.
141. Schaapveld M, Aleman BM, van Eggermond AM, et al. Second Cancer Risk Up to 40 Years after Treatment for Hodgkin's Lymphoma. *NEJM*. 2015;373: 2499-2511.
142. Moskowitz CS, Chou JF, Wolden SL, et al. Breast cancer after chest radiation therapy for childhood cancer. *J Clin Oncol*. 2014;32: 2217-2223.
143. Titus-Ernstoff L, Hatch EE, Hoover RN, et al. Long-term cancer risk in women given diethylstilbestrol (DES) during pregnancy. *Br J Cancer*. 2001;84: 126-133.
144. Hoover RN, Hyer M, Pfeiffer RM, et al. Adverse health outcomes in women exposed in utero to diethylstilbestrol. *N Engl J Med*. 2011;365: 1304-1314.
145. Ingber SZ, Buser MC, Pohl HR, Abadin HG, Murray HE, Scinicariello F. DDT/DDE and breast cancer: a meta-analysis. *Regul Toxicol Pharmacol*. 2013;67: 421-433.
146. Salehi F, Turner MC, Phillips KP, Wigle DT, Krewski D, Aronson KJ. Review of the etiology of breast cancer with special attention to organochlorines as potential endocrine disruptors. *J Toxicol Environ Health B Crit Rev*. 2008;11: 276-300.
147. Calle EE, Frumkin H, Henley SJ, Savitz DA, Thun MJ. Organochlorine and breast cancer risk. *CA Cancer J Clin*. 2002;52: 301-309.
148. Lopez-Cervantes M, Torres-Sanchez L, Tobias A, Lopez-Carrillo L. Dichlorodiphenyldichloroethane burden and breast cancer risk: a meta-analysis of the epidemiologic evidence. *Environ Health Perspect*. 2004;112: 207-214.
149. Cohn BA, La Merrill M, Krigbaum NY, et al. DDT Exposure in Utero and Breast Cancer. *J Clin Endocrinol Metab*. 2015;100: 2865-2872.
150. Brody JG, Moysich KB, Humblet O, Attfield KR, Beehler GP, Rudel RA. Environmental pollutants and breast cancer. *Cancer*. 2007;109: 2667-2711.
151. Jia Y, Lu Y, Wu K, et al. Does night work increase the risk of breast cancer? A systematic review and meta-analysis of epidemiological studies. *Cancer Epidemiol*. 2013;37: 197-206.
152. Hansen J. Night Shift Work and Risk of Breast Cancer. *Curr Environ Health Rep*. 2017.
153. Wegrzyn LR, Tamimi RM, Rosner BA, et al. Rotating night shift work and risk of breast cancer in the Nurses' Health Studies. *Amer J Epidemiol*. 2017.
154. Stevens RG, Brainard GC, Blask DE, Lockley SW, Motta ME. Breast cancer and circadian disruption from electric lighting in the modern world. *CA Cancer J Clin*. 2014;64: 207-218.
155. International Agency for Research on Cancer. *IARC monographs on the evaluation of carcinogenic risks to humans. Volume 98. Shift-work, painting and fire-fighting*. Lyon, France: International Agency for Research on Cancer, 2007.
156. ACOG Committee Opinion No. 434: induced abortion and breast cancer risk. *Obstet Gynecol*. 2009;113: 1417-1418.
157. Couzin J. Cancer risk. Review rules out abortion-cancer link. *Science*. 2003;299: 1498.
158. Chen L, Malone KE, Li CI. Bra wearing not associated with breast cancer risk: a population-based case-control study. *Cancer Epidemiol Biomarkers Prev*. 2014;23: 2181-2185.

159. Clemens MW, Miranda RN. Coming of Age: Breast Implant-Associated Anaplastic Large Cell Lymphoma After 18 Years of Investigation. *Clin Plastic Surg.* 2015;42: 605-613.
160. Llanos AAM, Rabkin A, Bandera EV, et al. Hair product use and breast cancer risk among African American and White women. *Carcinogenesis.* 2017.
161. Takkouche B, Etminan M, Montes-Martinez A. Personal use of hair dyes and risk of cancer: a meta-analysis. *JAMA.* 2005;293: 2516-2525.
162. Rosenberg L, Boggs DA, Adams-Campbell LL, Palmer JR. Hair relaxers not associated with breast cancer risk: evidence from the black women's health study. *Cancer Epidemiol Biomarkers Prev.* 2007;16: 1035-1037.
163. Mirick DK, Davis S, Thomas DB. Antiperspirant use and the risk of breast cancer. *J Natl Cancer Inst.* 2002;94: 1578-1580.
164. Gikas PD, Mansfield L, Mokbel K. Do underarm cosmetics cause breast cancer? *Int J Fertil Womens Med.* 2004;49: 212-214.
165. Cuzick J, Sestak I, Bonanni B, et al. Selective oestrogen receptor modulators in prevention of breast cancer: an updated meta-analysis of individual participant data. *Lancet.* 2013;381: 1827-1834.
166. Goss PE, Ingle JN, Ales-Martinez JE, et al. Exemestane for breast-cancer prevention in postmenopausal women. *N Engl J Med.* 2011;364: 2381-2391.
167. Cuzick J, Sestak I, Forbes JF, et al. Anastrozole for prevention of breast cancer in high-risk postmenopausal women (IBIS-II): an international, double-blind, randomised placebo-controlled trial. *Lancet.* 2014;383: 1041-1048.
168. Ludwig KK, Neuner J, Butler A, Geurts JL, Kong AL. Risk reduction and survival benefit of prophylactic surgery in BRCA mutation carriers, a systematic review. *Am J Surg.* 2016;212: 660-669.
169. Rebbeck TR, Kauff ND, Domchek SM. Meta-analysis of risk reduction estimates associated with risk-reducing salpingo-oophorectomy in BRCA1 or BRCA2 mutation carriers. *J Natl Cancer Inst.* 2009;101: 80-87.
170. Domchek SM, Friebel TM, Singer CF, et al. Association of risk-reducing surgery in BRCA1 or BRCA2 mutation carriers with cancer risk and mortality. *JAMA.* 2010;304: 967-975.
171. Kotsopoulos J, Huzarski T, Gronwald J, et al. Bilateral Oophorectomy and Breast Cancer Risk in BRCA1 and BRCA2 Mutation Carriers. *J Natl Cancer Inst.* 2017;109.
172. Oeffinger KC, Fontham ET, Etzioni R, et al. Breast Cancer Screening for Women at Average Risk: 2015 Guideline Update From the American Cancer Society. *JAMA.* 2015;314: 1599-1614.
173. Pisano ED, Hendrick RE, Yaffe MJ, et al. Diagnostic accuracy of digital versus film mammography: exploratory analysis of selected population subgroups in DMIST. *Radiology.* 2008;246: 376-383.
174. Kerlikowske K, Hubbard RA, Miglioretti DL, et al. Comparative effectiveness of digital versus film-screen mammography in community practice in the United States: a cohort study. *Ann Intern Med.* 2011;155: 493-502.
175. Souza FH, Wendland EM, Rosa MI, Polanczyk CA. Is full-field digital mammography more accurate than screen-film mammography in overall population screening? A systematic review and meta-analysis. *Breast.* 2013.
176. Friedewald SM, Rafferty EA, Rose SL, et al. Breast cancer screening using tomosynthesis in combination with digital mammography. *JAMA.* 2014;311: 2499-2507.
177. Bernardi D, Macaskill P, Pellegrini M, et al. Breast cancer screening with tomosynthesis (3D mammography) with acquired or synthetic 2D mammography compared with 2D mammography alone (STORM-2): a population-based prospective study. *Lancet Oncol.* 2016;17: 1105-1113.
178. Conant EF, Beaber EF, Sprague BL, et al. Breast cancer screening using tomosynthesis in combination with digital mammography compared to digital mammography alone: a cohort study within the PROSPER consortium. *Breast Cancer Res Treat.* 2016;156: 109-116.
179. Independent U. K. Panel on Breast Cancer Screening. The benefits and harms of breast cancer screening: an independent review. *Lancet.* 2012;380: 1778-1786.
180. Coldman A, Phillips N, Wilson C, et al. Pan-Canadian study of mammography screening and mortality from breast cancer. *J Natl Cancer Inst.* 2014;106.
181. Hofvind S, Ursin G, Tretli S, Sebuodegard S, Moller B. Breast cancer mortality in participants of the Norwegian Breast Cancer Screening Program. *Cancer.* 2013;119: 3106-3112.
182. Hubbard RA, Kerlikowske K, Flowers CI, Yankaskas BC, Zhu W, Miglioretti DL. Cumulative probability of false-positive recall or biopsy recommendation after 10 years of screening mammography: a cohort study. *Ann Intern Med.* 2011;155: 481-492.
183. Kerlikowske K, Zhu W, Hubbard RA, et al. Outcomes of screening mammography by frequency, breast density, and postmenopausal hormone therapy. *JAMA Intern Med.* 2013;173: 807-816.
184. Lehman CD, Arao RF, Sprague BL, et al. National Performance Benchmarks for Modern Screening Digital Mammography: Update from the Breast Cancer Surveillance Consortium. *Radiology.* 2017;283: 49-58.
185. Elmore JG, Barton MB, Moceri VM, Polk S, Arena PJ, Fletcher SW. Ten-year risk of false positive screening mammograms and clinical breast examinations. *N Engl J Med.* 1998;338: 1089-1096.
186. Gotzsche PC, Jorgensen KJ. Screening for breast cancer with mammography. *Cochrane Database Syst Rev.* 2013;6: CD001877.
187. Marmot MG, Altman DG, Cameron DA, Dewar JA, Thompson SG, Wilcox M. The benefits and harms of breast cancer screening: an independent review. *Br J Cancer.* 2013;108: 2205-2240.
188. Nelson HD, Tyne K, Naik A, et al. *Screening for Breast Cancer: Systematic Evidence Review Update for the US Preventive Services Task Force.* Rockville (MD), 2009.
189. Duffy SW, Tabar L, Olsen AH, et al. Absolute numbers of lives saved and overdiagnosis in breast cancer screening, from a randomized trial and from the Breast Screening Programme in England. *J Med Screen.* 2010;17: 25-30.
190. Puliti D, Zappa M, Miccinesi G, Falini P, Crocetti E, Paci E. An estimate of overdiagnosis 15 years after the start of mammographic screening in Florence. *Eur J Cancer.* 2009;45: 3166-3171.
191. Lauby-Secretan B, Scoccianti C, Loomis D, et al. Breast-cancer screening – viewpoint of the IARC Working Group. *N Engl J Med.* 2015;372: 2353-2358.
192. Yaffe MJ, Mainprize JG. Risk of radiation-induced breast cancer from mammographic screening. *Radiology.* 2011;258: 98-105.
193. de Gelder R, Draisma G, Heijnsdijk EA, de Koning HJ. Population-based mammography screening below age 50: balancing radiation-induced vs prevented breast cancer deaths. *Br J Cancer.* 2011;104: 1214-1220.

194. Brawley OW. Risk-based mammography screening: an effort to maximize the benefits and minimize the harms. *Ann Intern Med.* 2012;156: 662-663.
195. National Center for Health Statistics. National Health Interview Survey, 2015. Public-use data file and documentation. <http://www.cdc.gov/nchs/nhis.htm>.
196. Centers for Disease Control and Prevention (CDC). Behavioral Risk Factor Surveillance System Survey Data. Atlanta, Georgia: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, 2017.
197. Lantz PM, Mullen J. The National Breast and Cervical Cancer Early Detection Program: 25 Years of public health service to low-income women. *Cancer Causes Control.* 2015;26: 653-656.
198. Centers for Disease Control and Prevention. National Breast and Cervical Cancer Early Detection Program (NBCCEDP). Available from URL: <http://www.cdc.gov/cancer/nbccedp/about.htm> Accessed 05/20/2015.
199. Saslow D, Boetes C, Burke W, et al. American Cancer Society guidelines for breast screening with MRI as an adjunct to mammography. *CA Cancer J Clin.* 2007;57: 75-89.
200. Haas JS, Hill DA, Wellman RD, et al. Disparities in the use of screening magnetic resonance imaging of the breast in community practice by race, ethnicity, and socioeconomic status. *Cancer.* 2016;122: 611-617.
201. Tagliafico AS, Calabrese M, Mariscotti G, et al. Adjunct Screening With Tomosynthesis or Ultrasound in Women With Mammography-Negative Dense Breasts: Interim Report of a Prospective Comparative Trial. *J Clin Oncol.* 2016.
202. Bobo JK, Lee NC, Thames SF. Findings from 752,081 clinical breast examinations reported to a national screening program from 1995 through 1998. *J Natl Cancer Inst.* 2000;92: 971-976.
203. McDonald S, Saslow D, Alciati MH. Performance and reporting of clinical breast examination: a review of the literature. *CA Cancer J Clin.* 2004;54: 345-361.
204. Smith RA, Saslow D, Sawyer KA, et al. American Cancer Society guidelines for breast cancer screening: update 2003. *CA Cancer J Clin.* 2003;53: 141-169.
205. Thomas DB, Gao DL, Ray RM, et al. Randomized trial of breast self-examination in Shanghai: final results. *J Natl Cancer Inst.* 2002;94: 1445-1457.
206. Semiglazov VF, Moiseenko VM, Manikhas AG, et al. Interim results of a prospective randomized study of self-examination for early detection of breast cancer. *Vopr Onkol.* 1999;45: 265-271.
207. Francis A, Thomas J, Fallowfield L, et al. Addressing overtreatment of screen detected DCIS; the LORIS trial. *Eur J Cancer.* 2015;51: 2296-2303.
208. Elshof LE, Tryfonidis K, Slaets L, et al. Feasibility of a prospective, randomised, open-label, international multicentre, phase III, non-inferiority trial to assess the safety of active surveillance for low risk ductal carcinoma in situ – The LORD study. *Eur J Cancer.* 2015;51: 1497-1510.
209. ClinicalTrials.gov. Comparison of Operative to Monitoring and Endocrine Therapy (COMET) Trial For Low Risk DCIS: A Phase III Prospective Randomized Trial. Available from URL: <https://clinicaltrials.gov/ct2/show/study/NCT02926911> Accessed May 16, 2017.
210. Benson JR, Jatoi I, Toi M. Treatment of low-risk ductal carcinoma in situ: is nothing better than something? *Lancet Oncol.* 2016;17: e442-e451.
211. Wazir U, Wazir A, Wells C, Mokbel K. Pleomorphic lobular carcinoma in situ: Current evidence and a systemic review. *Oncol Lett.* 2016;12: 4863-4868.
212. Chen Y, Jiang L, Gao B, Cheng ZY, Jin J, Yang KH. Survival and disease-free benefits with mastectomy versus breast conservation therapy for early breast cancer: a meta-analysis. *Breast Cancer Res Treat.* 2016;157: 517-525.
213. Early Breast Cancer Trialists' Collaborative Group, Darby S, McGale P, et al. Effect of radiotherapy after breast-conserving surgery on 10-year recurrence and 15-year breast cancer death: meta-analysis of individual patient data for 10,801 women in 17 randomised trials. *Lancet.* 2011;378: 1707-1716.
214. van Maaren MC, de Munck L, de Bock GH, et al. 10 year survival after breast-conserving surgery plus radiotherapy compared with mastectomy in early breast cancer in the Netherlands: a population-based study. *Lancet Oncol.* 2016.
215. Hartmann-Johnsen OJ, Karesen R, Schlichting E, Nygard JF. Survival is Better After Breast Conserving Therapy than Mastectomy for Early Stage Breast Cancer: A Registry-Based Follow-up Study of Norwegian Women Primary Operated Between 1998 and 2008. *Ann Surg Oncol.* 2015;22: 3836-3845.
216. Hwang ES, Lichtensztajn DY, Gomez SL, Fowble B, Clarke CA. Survival after lumpectomy and mastectomy for early stage invasive breast cancer: the effect of age and hormone receptor status. *Cancer.* 2013;119: 1402-1411.
217. Agarwal S, Pappas L, Neumayer L, Kokeny K, Agarwal J. Effect of breast conservation therapy vs mastectomy on disease-specific survival for early-stage breast cancer. *JAMA Surg.* 2014;149: 267-274.
218. Smith BD, Jiang J, Shih YC, et al. Cost and Complications of Local Therapies for Early-Stage Breast Cancer. *J Natl Cancer Inst.* 2017;109.
219. Lautner M, Lin H, Shen Y, et al. Disparities in the Use of Breast-Conserving Therapy Among Patients With Early-Stage Breast Cancer. *JAMA Surg.* 2015;150: 778-786.
220. Kummerow KL, Du L, Penson DF, Shyr Y, Hooks MA. Nationwide trends in mastectomy for early-stage breast cancer. *JAMA surgery.* 2015;150: 9-16.
221. McGuire KP, Santillan AA, Kaur P, et al. Are mastectomies on the rise? A 13-year trend analysis of the selection of mastectomy versus breast conservation therapy in 5865 patients. *Ann Surg Oncol.* 2009;16: 2682-2690.
222. Bellavance EC, Kesmodel SB. Decision-Making in the Surgical Treatment of Breast Cancer: Factors Influencing Women's Choices for Mastectomy and Breast Conserving Surgery. *Front Oncol.* 2016;6: 74.
223. Freedman RA, Virgo KS, Labadie J, He Y, Partridge AH, Keating NL. Receipt of locoregional therapy among young women with breast cancer. *Breast Cancer Res Treat.* 2012;135: 893-906.
224. Wong SM, Freedman RA, Sagara Y, Aydogan F, Barry WT, Golshan M. Growing Use of Contralateral Prophylactic Mastectomy Despite no Improvement in Long-term Survival for Invasive Breast Cancer. *Ann Surg.* 2016.
225. Kurian AW, Lichtensztajn DY, Keegan TH, Nelson DO, Clarke CA, Gomez SL. Use of and mortality after bilateral mastectomy compared with other surgical treatments for breast cancer in California, 1998-2011. *JAMA.* 2014;312: 902-914.
226. Tuttle TM, Jarosek S, Habermann EB, et al. Increasing rates of contralateral prophylactic mastectomy among patients with ductal carcinoma in situ. *J Clin Oncol.* 2009;27: 1362-1367.

227. Fayanju OM, Stoll CR, Fowler S, Colditz GA, Margenthaler JA. Contralateral prophylactic mastectomy after unilateral breast cancer: a systematic review and meta-analysis. *Ann Surg*. 2014;260: 1000-1010.
228. Boughey JC, Attai DJ, Chen SL, et al. Contralateral Prophylactic Mastectomy (CPM) Consensus Statement from the American Society of Breast Surgeons: Data on CPM Outcomes and Risks. *Ann Surg Oncol*. 2016;23: 3100-3105.
229. Lyman GH, Somerfield MR, Bossner LD, Perkins CL, Weaver DL, Giuliano AE. Sentinel Lymph Node Biopsy for Patients With Early-Stage Breast Cancer: American Society of Clinical Oncology Clinical Practice Guideline Update. *J Clin Oncol*. 2016; JCO2016710947.
230. Giuliano AE, Ballman K, McCall L, et al. Locoregional Recurrence After Sentinel Lymph Node Dissection With or Without Axillary Dissection in Patients With Sentinel Lymph Node Metastases: Long-term Follow-up From the American College of Surgeons Oncology Group (Alliance) ACOSOG Z0011 Randomized Trial. *Ann Surg*. 2016;264: 413-420.
231. DiSipio T, Rye S, Newman B, Hayes S. Incidence of unilateral arm lymphoedema after breast cancer: a systematic review and meta-analysis. *Lancet Oncol*. 2013;14: 500-515.
232. Cheema BS, Kilbreath SL, Fahey PP, Delaney GP, Atlantis E. Safety and efficacy of progressive resistance training in breast cancer: a systematic review and meta-analysis. *Breast Cancer Res Treat*. 2014;148: 249-268.
233. Lawenda BD, Mondry TE, Johnstone PA. Lymphedema: a primer on the identification and management of a chronic condition in oncologic treatment. *CA Cancer J Clin*. 2009;59: 8-24.
234. Hughes KS, Schnaper LA, Berry D, et al. Lumpectomy plus tamoxifen with or without irradiation in women 70 years of age or older with early breast cancer. *N Engl J Med*. 2004;351: 971-977.
235. Haviland JS, Owen JR, Dewar JA, et al. The UK Standardisation of Breast Radiotherapy (START) trials of radiotherapy hypofractionation for treatment of early breast cancer: 10-year follow-up results of two randomised controlled trials. *Lancet Oncol*. 2013;14: 1086-1094.
236. Shaitelman SF, Schlembach PJ, Arzu I, et al. Acute and Short-term Toxic Effects of Conventionally Fractionated vs Hypofractionated Whole-Breast Irradiation: A Randomized Clinical Trial. *JAMA Oncol*. 2015;1: 931-941.
237. Shah C, Badiyan S, Ben Wilkinson J, et al. Treatment efficacy with accelerated partial breast irradiation (APBI): final analysis of the American Society of Breast Surgeons MammoSite(R) breast brachytherapy registry trial. *Ann Surg Oncol*. 2013;20: 3279-3285.
238. Strnad V, Ott OJ, Hildebrandt G, et al. 5-year results of accelerated partial breast irradiation using sole interstitial multicatheter brachytherapy versus whole-breast irradiation with boost after breast-conserving surgery for low-risk invasive and in-situ carcinoma of the female breast: a randomised, phase 3, non-inferiority trial. *Lancet*. 2016;387: 229-238.
239. Krug D, Baumann R, Budach W, et al. Current controversies in radiotherapy for breast cancer. *Radiat Oncol*. 2017;12: 25.
240. Shah C, Tendulkar R, Smile T, et al. Adjuvant Radiotherapy in Early-Stage Breast Cancer: Evidence-Based Options. *Ann Surg Oncol*. 2016;23: 3880-3890.
241. Zhang L, Zhou Z, Mei X, et al. Intraoperative Radiotherapy Versus Whole-Breast External Beam Radiotherapy in Early-Stage Breast Cancer: A Systematic Review and Meta-Analysis. *Medicine*. 2015;94: e1143.
242. Mauri D, Pavlidis N, Ioannidis JP. Neoadjuvant versus adjuvant systemic treatment in breast cancer: a meta-analysis. *J Natl Cancer Inst*. 2005;97: 188-194.
243. Carey LA, Dees EC, Sawyer L, et al. The triple negative paradox: primary tumor chemosensitivity of breast cancer subtypes. *Clin Cancer Res*. 2007;13: 2329-2334.
244. Sparano JA, Gray RJ, Makower DF, et al. Prospective Validation of a 21-Gene Expression Assay in Breast Cancer. *N Engl J Med*. 2015;373: 2005-2014.
245. Early Breast Cancer Trialists' Collaborative Group, Davies C, Godwin J, et al. Relevance of breast cancer hormone receptors and other factors to the efficacy of adjuvant tamoxifen: patient-level meta-analysis of randomised trials. *Lancet*. 2011;378: 771-784.
246. Davies C, Pan H, Godwin J, et al. Long-term effects of continuing adjuvant tamoxifen to 10 years versus stopping at 5 years after diagnosis of oestrogen receptor-positive breast cancer: ATLAS, a randomised trial. *Lancet*. 2013;381: 805-816.
247. Burstein HJ, Temin S, Anderson H, et al. Adjuvant endocrine therapy for women with hormone receptor-positive breast cancer: American Society of Clinical Oncology clinical practice guideline focused update. *J Clin Oncol*. 2014;32: 2255-2269.
248. Dowsett M, Cuzick J, Ingle J, et al. Meta-analysis of breast cancer outcomes in adjuvant trials of aromatase inhibitors versus tamoxifen. *J Clin Oncol*. 2010;28: 509-518.
249. Pagani O, Regan MM, Walley BA, et al. Adjuvant exemestane with ovarian suppression in premenopausal breast cancer. *N Engl J Med*. 2014;371: 107-118.
250. Klijn JG, Blamey RW, Boccardo F, et al. Combined tamoxifen and luteinizing hormone-releasing hormone (LHRH) agonist versus LHRH agonist alone in premenopausal advanced breast cancer: a meta-analysis of four randomized trials. *J Clin Oncol*. 2001;19: 343-353.
251. Romond EH, Perez EA, Bryant J, et al. Trastuzumab plus adjuvant chemotherapy for operable HER2-positive breast cancer. *N Engl J Med*. 2005;353: 1673-1684.
252. Runowicz CD, Leach CR, Henry NL, et al. American Cancer Society/American Society of Clinical Oncology Breast Cancer Survivorship Care Guideline. *CA Cancer J Clin*. 2016;66: 43-73.
253. Copeland G, Lake A, Firth R, et al. *Cancer in North America: 2010-2014. Volume Two: Registry-specific Cancer Incidence for the United States, Canada and North America*. Springfield, IL: North American Association of Central Cancer Registries, Inc, June 2017.
254. Copeland G, Lake A, Firth R, et al. *Cancer in North America: 2010-2014. Volume One: Combined Cancer Incidence for the United States, Canada and North America*. Springfield, IL: North American Association of Central Cancer Registries, Inc, June 2017.
255. Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database: Incidence – SEER 9 Regs Research Data, Nov 2016 Sub (1973-2014) <Katrina/Rita Population Adjustment> Total U.S., 1969-2015 Counties, National Cancer Institute, DCCPS, Surveillance Research Program, released April 2017, based on the November 2016 submission.
256. Surveillance Research Program, National Cancer Institute. SEER*Stat Software. Version 8.3.4. Bethesda, MD: National Cancer Institute; 2017.
257. DevCan: Probability of Developing or Dying of Cancer Software, Version 6.7.5; Statistical Research and Applications Branch, National Cancer Institute, 2017. <https://surveillance.cancer.gov/devcan/>.

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