

Breast Cancer Facts & Figures 2019-2020



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Breast Cancer Basic Facts

What is breast cancer?

Breast cancer is a group of diseases in which cells in breast tissue change and divide uncontrolled, typically resulting in a lump or mass. Most breast cancers begin in the lobules (milk glands) or in the ducts that connect the lobules to the nipple.

What are the signs and symptoms of breast cancer?

Breast cancer typically has 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 changes, such as spontaneous discharge (especially if bloody), scaliness, or retraction. Any persistent change in the breast should be evaluated by a physician.

How is breast cancer diagnosed?

Breast cancer is typically detected either during screening, 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). When cancer is suspected, tissue for microscopic analysis is usually obtained from a needle biopsy (fine-needle or larger core-needle) and less often from a surgical biopsy. 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 extent of the cancer and its spread at the time of diagnosis determines its stage, which is essential for guiding treatment options and prognosis (prediction of disease outcome). The two main staging systems for cancer are the American Joint Committee on Cancer (AJCC) staging system, typically used in clinical settings, and the Surveillance, Epidemiology, and End Results (SEER) summary staging system, used for descriptive and statistical analysis of tumor registry data. The AJCC system was recently updated (effective January 2018) to add prognostic stage groups.¹ AJCC anatomic stage is based on extent of the cancer (in the breast, regional lymph nodes, and distant spread), while prognostic stage also includes information on the presence of estrogen receptors (ER), progesterone receptors (PR), levels of human epidermal growth factor receptor 2 (HER2, a growth-promoting protein) and/or extra copies of the HER2 gene (HER2+/HER2-), and grade (reflecting how closely the cancer's microscopic appearance looks like normal breast tissue). In this document, we generally refer to the SEER summary stage except in the section on the description of breast cancer treatment (page 23), which references AJCC anatomic stage.

According to the SEER summary stage system:

- In situ stage refers to the presence of abnormal cells that are confined to the layer of cells where they originated.
- Local stage refers to invasive cancer that is confined to the breast.
- Regional stage refers to cancer that has spread to surrounding tissue and/or nearby lymph nodes.
- Distant stage refers to cancer that has spread to distant organs and/or lymph nodes, including nodes above the collarbone.

What are the types of breast cancer?

In Situ

Historically, ductal carcinoma in situ (DCIS) and lobular carcinoma in situ (LCIS), also known as lobular neoplasia, were considered the two main types of in situ breast cancer. However, LCIS is generally believed to be a benign condition associated with increased breast cancer risk, but without the potential to progress to invasive cancer, so it was removed from the latest edition of the AJCC breast cancer staging system.² DCIS, on the other hand, is a precursor to invasive cancer, although not all DCIS progresses. In fact, DCIS sometimes grows so slowly that even without treatment it would not affect a woman's health. Long-term studies have found that only 20%-53% of women with untreated DCIS are ultimately diagnosed with invasive breast cancer.³⁻⁵ DCIS patients who are premenopausal at diagnosis or who had their DCIS detected by palpation are at greater risk of being diagnosed with a future invasive breast cancer.^{6,7} During 2012-2016, DCIS represented 16% of all breast cancer diagnoses.⁸

See page 13 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*.

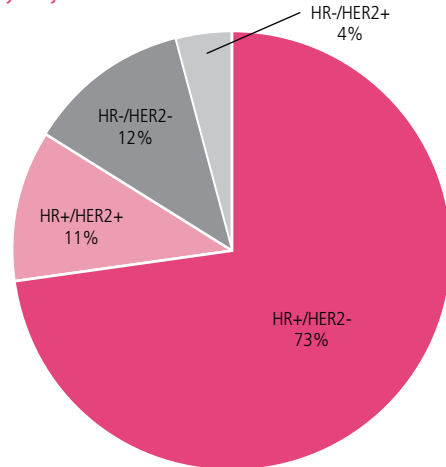
Invasive

Most (81%) breast cancers are invasive, or infiltrating, which means the abnormal cells have broken through the walls of the glands or ducts where they originated and grown into surrounding breast tissue. Although breast cancer was historically referred to as a single disease, it is now considered a group of diseases, consisting of four major molecular subtypes and at least 21 distinct histological subtypes (type of tissue in which the cancer originates) that differ in risk factors, presentation, response to treatment, and outcomes.

Histologic subtypes

Histology is based on the size, shape, and arrangement of breast cancer cells. More than 75% of invasive breast cancers are now histologically categorized as “no special type,” historically called “ductal” carcinomas.⁸ The most common special histologic subtype is invasive lobular

Figure 1. Distribution of Female Breast Cancer Subtypes, US, 2012-2016



HR = hormone receptor, HER2 = human epidermal growth factor receptor 2.
Source: North American Association of Central Cancer Registries (NAACCR), 2019.
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carcinoma, representing about 15% of invasive breast cancers.⁸ Tubular, mucinous, cribriform, and papillary carcinoma are rare breast cancer subtypes that are generally associated with favorable prognoses.⁹ Inflammatory breast cancer is an uncommon but aggressive type of breast cancer that is characterized by swelling and redness of the skin of the breast.

Molecular subtypes

Breast cancer molecular subtypes are determined through gene expression analysis, a costly and complicated process that is not currently standard clinical practice. However, these subtypes can be approximated using routine methods for clinical evaluation of biological markers (ER, PR, HER2, and sometimes others). Hormone receptor positive (HR+) cancers are those that test positive for ER or PR, or both. Information about grade and proliferation (rate of cell division) is also sometimes used to assign subtype.

The four main molecular subtypes are described below. It is worth noting that there are overlaps between categories and the clinical approximations do not perfectly correspond to the molecular breast cancer subtypes as described on the next page.¹⁰

Luminal A (HR+/HER2-): This is the most common type of breast cancer (Figure 1) and tends to be slower-growing and less aggressive than other subtypes. Luminal A tumors are associated with the most favorable prognosis in part because they are usually responsive to hormonal therapy (see page 26).^{11, 12}

Luminal B (HR+/HER2+): In addition to being HR+, this subtype was originally characterized clinically as always being positive for HER2, but more recently has been defined by being highly positive for the protein Ki67 (an indicator of a large number of actively dividing cells) and/or HER2. Luminal B breast cancers tend to be higher grade than luminal A and thus are associated with poorer outcomes.^{11, 12}

Basal-like (HR-/HER2-): These cancers are also called triple negative because they are ER-, PR- and HER2-. The

majority (about 75%) of triple negative breast cancers fall in to the basal-like subtype defined by gene expression profiling.¹³ Triple negative breast cancers have a poorer prognosis than other subtypes, in part because treatment advances have lagged behind other molecular subtypes.^{14, 15} These cancers occur at twice the rate in black women compared to white women in the US, and are also more common in premenopausal women and those with a *BRCA1* gene mutation.¹⁶

HER2-enriched (HR-/HER2+): In the past, this subtype had the worst prognosis; however, the widespread use of targeted therapies for HER2+ cancers has substantially improved outcomes for these patients.^{14, 17} For more information about the treatment of HER2+ breast cancers, see the section on targeted therapy on page 26.

Breast Cancer Occurrence

How many cases and deaths are expected to occur in 2019?

In 2019, an estimated 268,600 new cases of invasive breast cancer will be diagnosed among women (Table 1) and approximately 2,670 cases will be diagnosed in men. In addition, an estimated 48,100 cases of DCIS will be diagnosed among women. Approximately 41,760 women and 500 men are expected to die from breast cancer in 2019.

Table 1. Estimated New DCIS and Invasive Breast Cancer Cases and Deaths among Women by Age, US, 2019

Age	DCIS cases		Invasive cases		Deaths	
	Number	%	Number	%	Number	%
<40	1,180	2%	11,870	4%	1,070	3%
40-49	8,130	17%	37,150	14%	3,250	8%
50-59	12,730	26%	61,560	23%	7,460	18%
60-69	14,460	30%	74,820	28%	9,920	24%
70-79	8,770	18%	52,810	20%	8,910	21%
80+	2,830	6%	30,390	11%	11,150	27%
All ages	48,100		268,600		41,760	

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

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How many women alive today have ever had breast cancer?

More than 3.8 million US women with a history of breast cancer were alive on January 1, 2019.¹⁸ Some of these women were cancer-free, while others still had evidence of cancer and may have been undergoing treatment. More than 150,000 breast cancer survivors are living with metastatic disease, three-fourths of whom were originally diagnosed with stage I-III.¹⁹

What is the risk of being diagnosed with breast cancer?

Approximately 1 in 8 women (13%) will be diagnosed with invasive breast cancer in their lifetime and 1 in 39 women (3%) will die from breast cancer (Table 2).²⁰ Lifetime risk is an average of risk for all women and accounts for deaths from other causes that may preempt a breast cancer diagnosis.

Breast cancer risk varies by age and race/ethnicity:

Table 2. Age-specific Ten-year Probability of Breast Cancer Diagnosis or Death for US Women

Current age	Diagnosed with invasive breast cancer	Dying from breast cancer
20	0.1% (1 in 1,479)	<0.1% (1 in 18,503)
30	0.5% (1 in 209)	<0.1% (1 in 2,016)
40	1.5% (1 in 65)	0.2% (1 in 645)
50	2.4% (1 in 42)	0.3% (1 in 310)
60	3.5% (1 in 28)	0.5% (1 in 193)
70	4.1% (1 in 25)	0.8% (1 in 132)
80	3.0% (1 in 33)	1.0% (1 in 101)
Lifetime risk	12.8% (1 in 8)	2.6% (1 in 39)

Note: Probability is among those who have not been previously diagnosed with cancer. Percentages and "1 in" numbers may not be numerically equivalent due to rounding.

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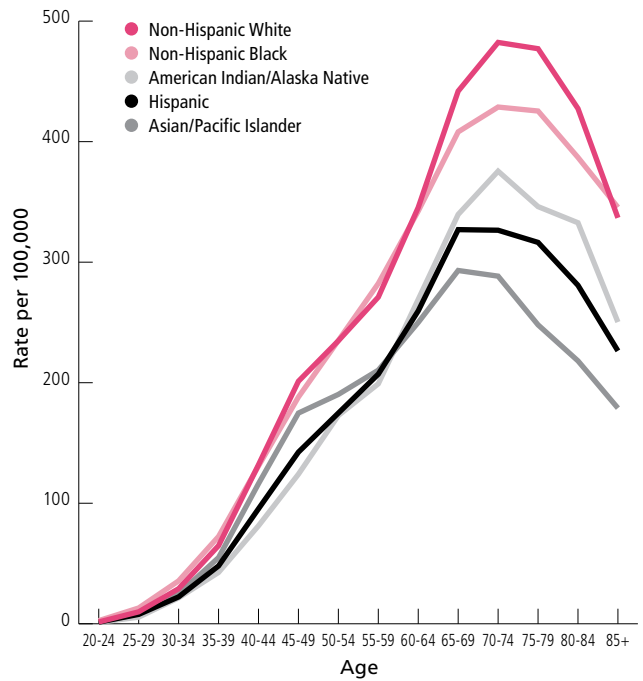
Age

- Breast cancer incidence and death rates increase with age until the seventh decade (Figure 2). 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 2012-2016, the median age at the time of breast cancer diagnosis was 62.²⁰ 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 was slightly younger for black women (60) than white women (63).²⁰
- Table 2 provides 10-year probabilities of invasive breast cancer diagnosis or death for women of different ages. By 10-year age groups, the probability of a breast cancer diagnosis is highest for women in their 70s (4.1%), while breast cancer death is most likely among women in their 80s (1.0%).

Race/Ethnicity

- Breast cancer incidence and death rates by race and ethnicity during the most recent time period are shown in Figure 3. Incidence rates are highest among non-Hispanic (NH) whites (130.8 per 100,000), followed closely by NH blacks (126.7). However, NH black women have the highest breast cancer death rate (28.4 deaths per 100,000), more than double that in Asian/Pacific Islander (API) women (11.5), who have the lowest incidence and death rates.

Figure 2. Age-specific Female Breast Cancer Incidence Rates by Race/Ethnicity, US, 2012-2016



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

Source: NAACCR, 2019. Data for American Indians/Alaska Natives are based on Purchased/Referred Care Delivery Area (PRCDA) counties.

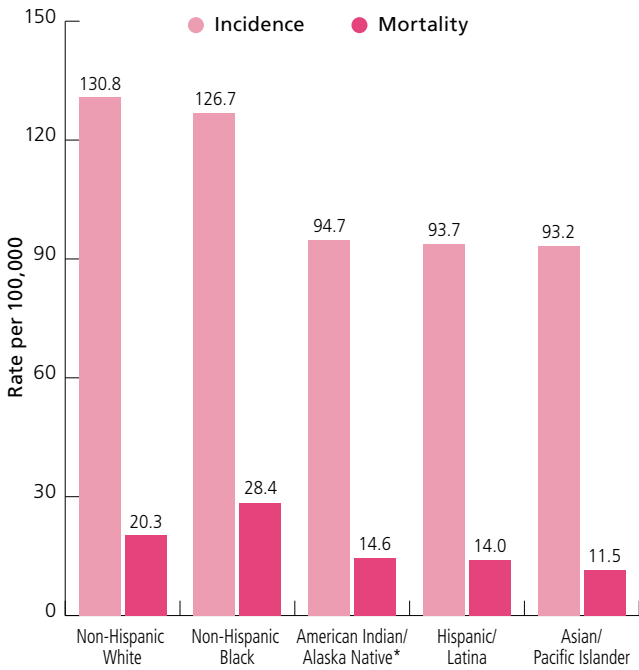
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- NH black women have higher incidence rates than NH whites before age 40 (Figure 2) and are more likely to die from breast cancer at every age.
- The distributions of breast cancer subtypes for the major racial/ethnic groups are shown in Figure 4. HR+/HER2- breast cancers are by far the most common subtype among women of all races/ethnicities. About 21% of breast cancers in NH black women are triple negative, which is about double the proportion of this subtype in other racial/ethnic groups. The higher breast cancer death rate in black women in part reflects the disproportionate burden of triple negative breast cancers in this group.

Stage

- At the time of diagnosis, approximately 64% of breast cancer patients have local-stage breast cancer, 27% have regional stage, and 6% have distant (metastatic) disease.

Figure 3. Female Breast Cancer Incidence (2012-2016) and Death (2013-2017) Rates by Race/Ethnicity, US

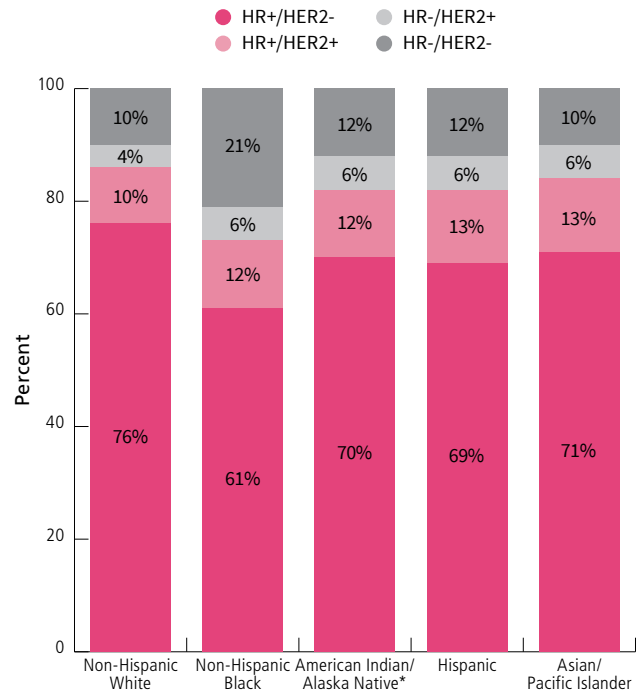


*Statistics based on data from PRCA counties. Note: Rates are per 100,000 and age adjusted to the 2000 US standard population.

Sources: Incidence – NAACCR, 2019. Mortality – National Center for Health Statistics (NCHS), Centers for Disease Control and Prevention, 2019.

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Figure 4. Distribution of Breast Cancer Subtypes by Race/Ethnicity, Ages 20 and Older, US, 2012-2016



HR = hormone receptor, HER2 = human epidermal growth factor receptor 2. Statistics based on data from PRCA counties.

Source: NAACCR, 2019.

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- Stage at diagnosis also varies by race/ethnicity (Figure 5). NH black, Hispanic, and American Indian/Alaska Native (AIAN) patients are less likely to be diagnosed with local-stage disease (56%-60%) compared to NH white and API patients (64%-66%).

How has the occurrence of breast cancer changed over time?

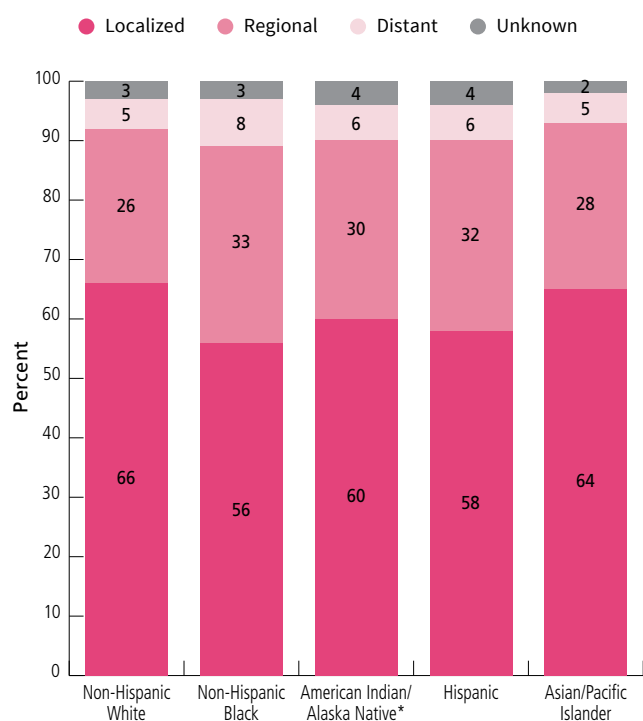
Incidence

Incidence rates of DCIS and invasive breast cancer rose rapidly during the 1980s and 1990s (Figure 6), particularly among women 50 years of age and older, largely due to increases in the prevalence of mammography screening, which increased from 29% in 1987 to 70% in 2000.²¹ For example, DCIS rates among women 50 and older, increased more than 11-fold from 1980 (7 cases per 100,000) to 2008 (83 cases per 100,000).

In contrast, there was a sharp drop (nearly 13%) in the invasive breast cancer rate between 1999 and 2004, believed to be largely 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 menopausal hormone users, and may also reflect small declines in mammography screening since 2000.^{22, 23} The decline in breast cancer incidence occurred primarily in white women, in those 50 years of age and older, and for ER+ disease.^{22, 24}

In the most recent time period (2012-2016), the DCIS rate declined by 2.1% per year⁸ and the invasive breast cancer incidence rate rose by about 0.3% per year.²⁰ In fact, the incidence rate for invasive breast cancer has been slowly increasing since 2004.²⁰ A recent study concluded that increases in body mass index (BMI) and declines in the average number of births per woman (both breast cancer risk factors) have likely contributed to the recent increase in incidence.²⁵

Figure 5. Female Breast Cancer Stage Distribution, by Race/Ethnicity, Ages 20 and Older, US, 2012-2016



*Statistics based on data from PRCA counties.

Source: NAACCR, 2019.

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Race/Ethnicity

Figure 7 presents trends in invasive female breast cancer incidence rates by race and ethnicity since 2001 based on data from 45 states, representing 92% of the US population. During the most recent 5 years of available data (2012 to 2016), overall breast cancer incidence rates increased most rapidly among APIs (1.5% per year), followed by AIANs (0.8% per year), and NH blacks and NH whites (both 0.5% per year), but were relatively stable in Hispanics.

Stage

The overall increase in breast cancer incidence is largely because of an increase in local-stage disease. From 2012 to 2016, the incidence rate increased by 1.1% per year for local-stage breast cancer, but declined by 0.8% per year for regional-stage disease, which may reflect a shift toward earlier stage at diagnosis. The incidence rate for distant-stage disease increased 2.5% annually during

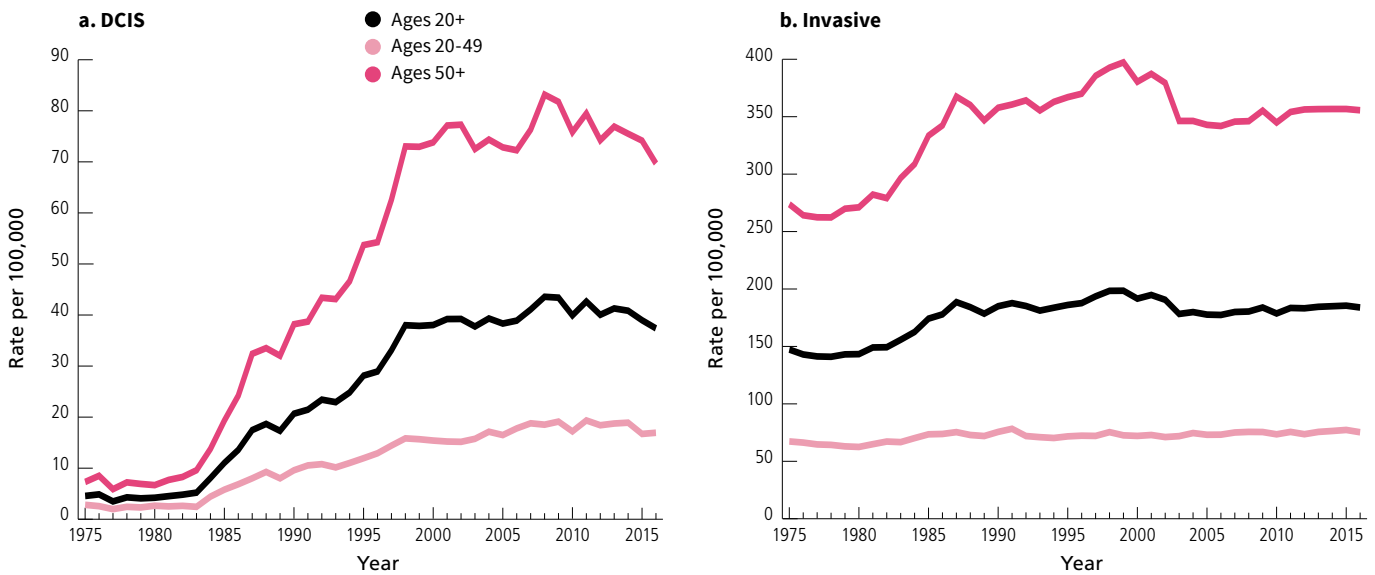
2001-2011, but has since stabilized. The increase in distant-stage disease may be partly explained by the decrease in unknown stage, because of more complete staging of advanced tumors.²⁶ This trend may also reflect increased detection of asymptomatic metastases due to the rise in the use of advanced imaging.

Mortality

The overall breast cancer death rate increased by 0.4% per year from 1975 to 1989, but since has decreased rapidly, for a total decline of 40% through 2017. As a result, 375,900 breast cancer deaths were averted in US women from 1989 to 2017. However, the decline in breast cancer mortality has slowed slightly in the most recent time period, from an annual decrease of 1.9% during 1988-2011 to 1.3% during 2011-2017. By race/ethnicity, the breast cancer death rate during 2013-2017 declined annually by 2.1% in Hispanics, 1.5% in NH blacks, 1.0% in NH whites, and 0.8% in APIs, but was stable in AIANs (Figure 8).

The decline in breast cancer mortality has been attributed to both improvements in treatment and earlier detection.²⁷ However, not all women have benefited equally from these advances, as indicated by the striking divergence in mortality trends between black and white women beginning in the early 1980s (Figure 8). This disparity likely reflects a combination of factors that are difficult to parse, including later stage at diagnosis and other unfavorable tumor characteristics, higher prevalence of obesity and other health conditions, less access to high-quality prevention, early detection, and treatment.^{28,29} For example, black women are more likely to be screened at lower resourced and nonaccredited facilities and also experience longer intervals between mammograms, and between abnormal results and follow-up.³⁰⁻³³ Although self-reported screening rates based on national surveys are similar between black and white women, studies indicate that black (and Hispanic) women are more likely than white women to overestimate their screening history.³⁴⁻³⁶ The black-white disparity has grown as treatment for breast cancers has improved (particularly for HR+ breast cancers), but appears to have peaked in 2011, when rates in NH black

Figure 6. Trends in Incidence Rates of Ductal Carcinoma In Situ and Invasive Female Breast Cancer by Age, US, 1975-2016



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

Source: Surveillance, Epidemiology, and End Results (SEER) Program, SEER 9 Registries, National Cancer Institute, 2019.

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women were 44% higher than those in whites. In the most recent period (2013-2017), the breast cancer death rate was 40% higher in black women versus white women (Figure 3).

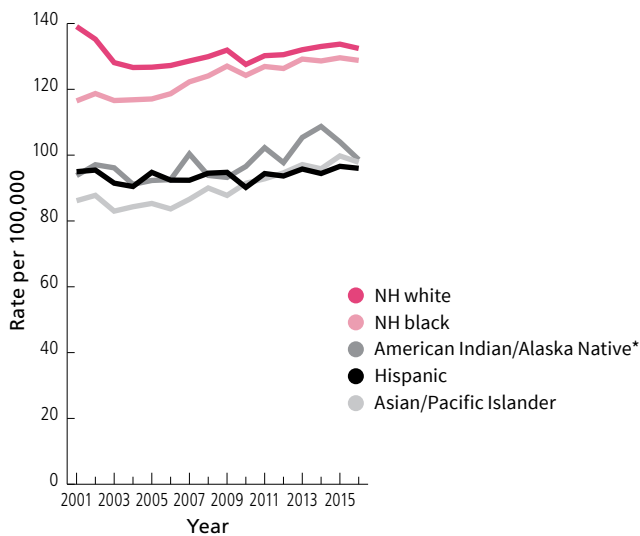
Are there geographic differences in breast cancer patterns?

Table 3 shows 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 NH white women compared to NH black women, rates are higher in NH black women in 4 of the 43 states with reliable data for both groups (Louisiana, Mississippi, Oklahoma, and Wisconsin), and are not statistically different in 26 other states and the District of Columbia.³⁷ Data for AIAN women are too sparse to provide by state; however, during 2012-2016, incidence rates were more than two-fold higher among women in Alaska (139.7 per 100,000) and the Southern Plains (150.8 per 100,000) compared to those living in the Southwest US (60.4 per 100,000).⁸

In contrast to incidence, breast cancer death rates are higher among NH black women than NH white women in every state, with rates in some states (e.g., Louisiana and Mississippi) as much as 60% higher (Table 3). Death rates reflect both cancer incidence and survival. Breast cancer mortality rates among NH white women tend to be highest in the North Central, Mid-Atlantic, and Western regions of the US (Figure 9). Among NH black women, the highest death rates are found in some of the South Central and Mid-Atlantic states, as well as California. Factors that contribute to geographic disparities include variations in risk factors and access to screening and treatment, which are influenced by socioeconomic factors, legislative policies, and proximity to medical services.

During 2013-2017, breast cancer death rates decreased in all states except Nebraska.³⁷ In addition, the decline in breast cancer mortality has leveled off for black women in Colorado and Wisconsin and for white women in Nebraska, Texas, and Virginia. Notably, during 2016-2017, breast cancer was the leading cause of cancer deaths (surpassing lung cancer) in 6 states (Arizona, Colorado, Florida, Georgia, Mississippi, and South Carolina) among black women and in Utah among white women.³⁷

Figure 7. Trends in Female Breast Cancer Incidence Rates by Race/Ethnicity, US, 2001-2016

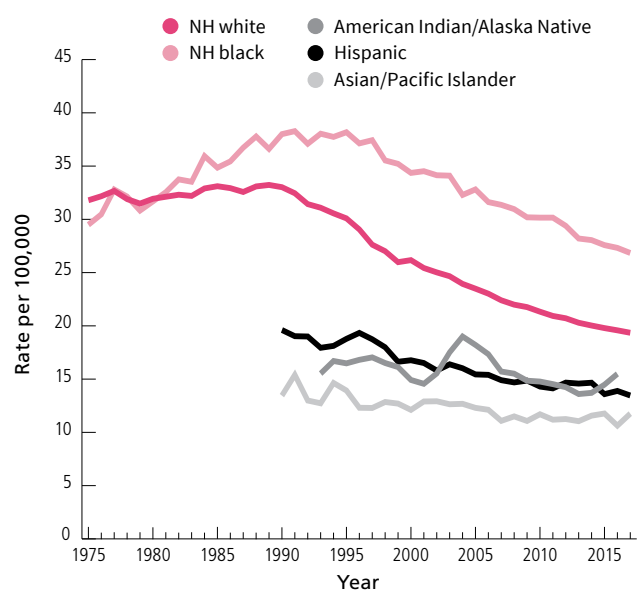


NH indicates non-Hispanic. *Statistics based on data from PRCDA counties. Note: Rates are per 100,000 and age adjusted to the 2000 US standard population. Rates were adjusted for reporting delays.

Source: NAACCR, 2019.

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Figure 8. Trends in Female Breast Cancer Death Rates by Race/Ethnicity, US, 1975-2017



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

Source: NCHS 2019. Rates for American Indian/Alaska Native are based on the PRCDA counties and are 3-year moving averages.

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Breast cancer survival

Relative survival rates are an estimate of the percentage of patients who will survive their cancer for a given period of time after 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.

Relative survival rates should be interpreted with caution because 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. In addition, long-term survival rates are based on data from patients diagnosed and treated many years ago and thus, do not reflect more recent improvements in early detection and treatment.

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

- 91% at 5 years after diagnosis
- 84% after 10 years
- 80% after 15 years

Stage at diagnosis

Stage at diagnosis is one of the most important factors affecting prognosis. Five-year relative survival rates for breast cancer are:

- 99% for localized disease
- 86% for regional disease
- 27% for patients diagnosed with metastatic disease²⁰

Breast cancer subtype (HR/HER2)

Breast cancer survival also varies by tumor subtype.

Five-year relative survival rates are:

- 92% for HR+/HER2-
- 89% for HR+/HER2+
- 83% for HR-/HER2+
- 77% for HR-/HER2-

Importantly, a recent study found that 4-year relative survival was 95% or greater for patients diagnosed with stage I breast cancers across all breast cancer subtypes.¹¹

Table 3. Female Breast Cancer Incidence and Death Rates by Race/Ethnicity and State

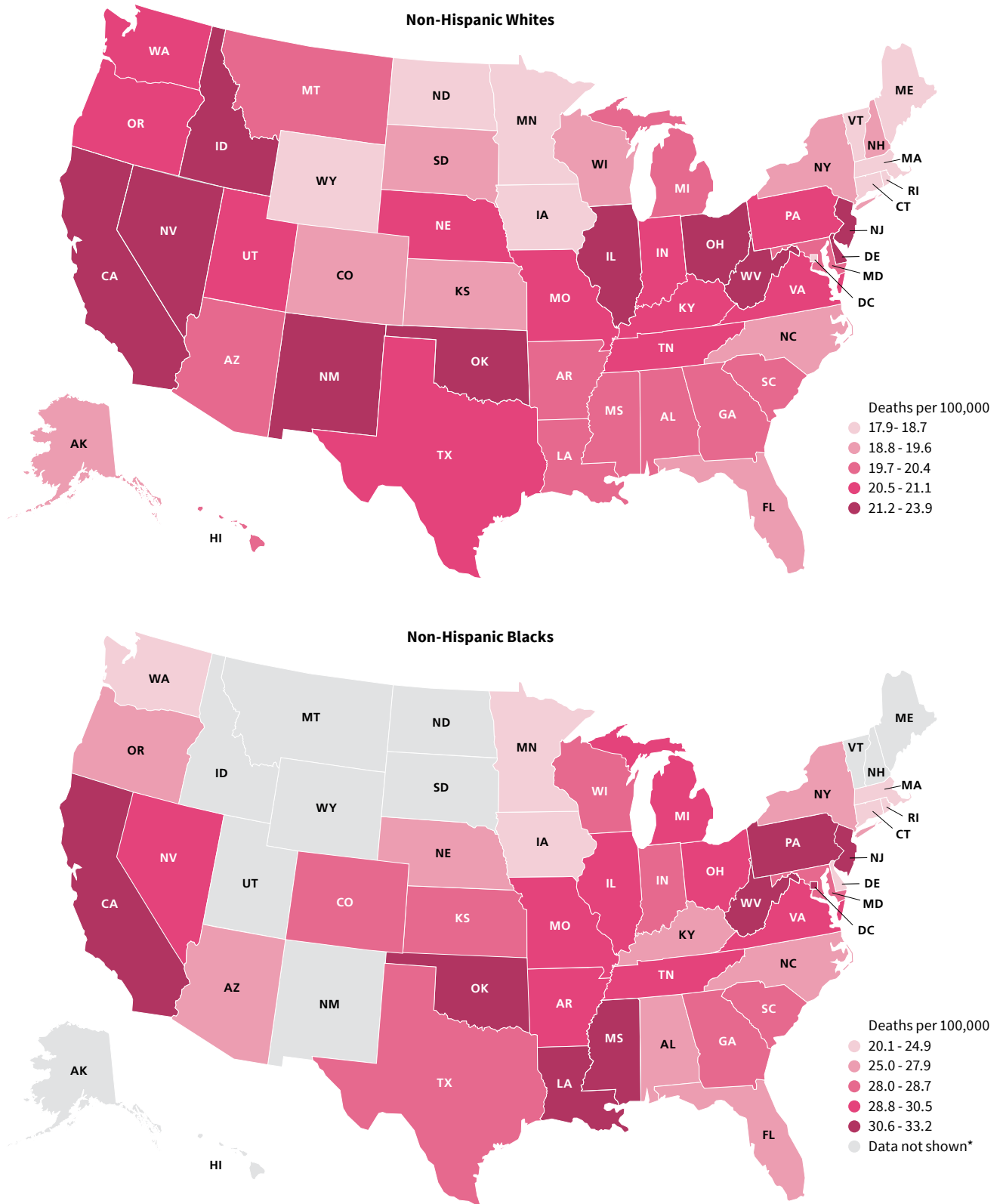
State	Incidence Rates (2012-2016)				Death Rates (2013-2017)			
	Non-Hispanic White	Non-Hispanic Black	Hispanic	Asian/Pacific Islander	Non-Hispanic White	Non-Hispanic Black	Hispanic	Asian/Pacific Islander
Alabama	121.2	125.7	57.1	81.5	20.0	26.8	*	*
Alaska	122.5	132.0	111.0	77.6	19.5	*	*	*
Arizona	122.1	111.7	91.9	80.4	20.0	26.0	15.2	12.1
Arkansas	116.3	118.3	92.2	117.3	19.9	29.5	13.2	*
California	138.8	128.1	91.4	98.0	22.2	30.9	14.4	12.9
Colorado	130.0	120.2	106.4	75.4	19.1	28.7	17.2	7.7
Connecticut	144.3	127.2	122.6	88.2	18.0	21.8	12.2	8.2
Delaware	139.1	135.7	101.6	92.3	21.2	24.8	*	*
District of Columbia†	139.9	135.5	69.9	86.3	18.1	33.2	*	*
Florida	123.4	110.1	99.2	75.4	19.5	25.6	14.2	9.9
Georgia	127.2	129.3	103.0	84.0	20.0	28.6	11.6	10.0
Hawaii	147.0	110.7	150.8	134.7	20.2	*	22.0	14.5
Idaho	125.7	*	94.7	86.2	22.4	*	13.1	*
Illinois	138.0	135.3	93.0	94.6	21.2	30.2	11.5	11.5
Indiana	123.1	129.1	91.5	71.2	20.6	28.3	14.0	*
Iowa	126.1	112.6	67.0	81.7	18.7	20.3	12.6	*
Kansas	127.8	125.4	88.5	73.6	19.2	28.3	11.9	*
Kentucky	127.2	128.3	71.5	73.3	21.1	25.2	*	*
Louisiana	122.8	134.7	90.1	69.0	19.9	32.3	9.6	*
Maine	126.1	*	82.5	75.4	18.5	*	*	*
Maryland	136.7	133.2	92.6	88.5	20.3	28.2	10.0	9.8
Massachusetts	143.3	120.7	88.2	93.1	18.1	20.1	11.5	7.9
Michigan	124.7	127.0	76.9	86.5	20.0	28.8	13.6	9.2
Minnesota	132.4	102.0	111.6	74.7	18.1	20.3	11.0	7.8
Mississippi	116.4	122.2	44.9	76.7	19.8	31.6	*	*
Missouri	130.0	133.7	76.3	94.3	20.8	30.5	10.8	12.1
Montana	124.0	*	125.0	115.7	19.9	*	*	*
Nebraska	127.8	107.5	93.2	57.7	20.6	25.8	*	*
Nevada†	120.9	109.5	79.4	80.1	23.9	29.7	12.0	15.0
New Hampshire	146.4	94.0	95.0	88.3	19.3	*	*	*
New Jersey	143.2	132.2	105.8	96.5	21.6	31.0	12.9	10.4
New Mexico	123.0	110.8	102.0	75.3	21.8	*	17.3	*
New York	141.9	121.7	102.3	94.1	19.4	25.3	13.4	9.8
North Carolina	134.8	133.9	81.5	80.7	19.5	27.8	10.4	11.2
North Dakota	127.5	*	*	*	18.2	*	*	*
Ohio	128.8	128.4	64.9	82.1	21.7	29.8	11.6	10.7
Oklahoma	118.2	126.9	91.3	83.7	22.5	31.3	11.9	*
Oregon	127.8	127.6	97.0	86.2	20.6	27.9	13.2	10.2
Pennsylvania	134.8	130.5	91.9	75.6	20.7	30.8	11.1	10.3
Rhode Island	144.1	118.9	86.6	85.3	18.2	24.8	*	*
South Carolina	130.9	128.6	91.2	73.8	19.7	28.0	8.4	*
South Dakota	132.6	*	*	*	19.3	*	*	*
Tennessee	123.8	124.8	70.7	72.6	20.6	29.8	13.4	13.2
Texas	123.5	120.9	89.1	71.3	20.5	28.5	15.5	10.1
Utah	116.4	80.6	106.5	96.2	20.8	*	11.1	15.0
Vermont	132.6	*	*	*	17.9	*	*	*
Virginia	131.8	134.6	79.0	79.3	21.0	28.9	10.0	9.5
Washington	139.1	124.1	101.1	99.7	20.9	22.8	10.4	11.9
West Virginia	117.5	128.2	*	94.7	21.8	31.2	*	*
Wisconsin	132.0	141.1	82.6	78.9	19.0	28.0	7.9	*
Wyoming	114.9	*	83.0	*	18.5	*	*	*
United States	130.8	126.7	93.7	93.2	20.3	28.4	14.0	11.5

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 registry did not achieve high-quality data standards for one or more years during 2012-2016 and are not included in the overall US incidence rate.

Sources: Incidence: NAACCR, 2019. Mortality: NCHS, 2019.

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Figure 9. Geographic Variation in Female Breast Cancer Death Rates by Race/Ethnicity, 2013-2017



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 2013-2017. Source: NCHS, 2019.

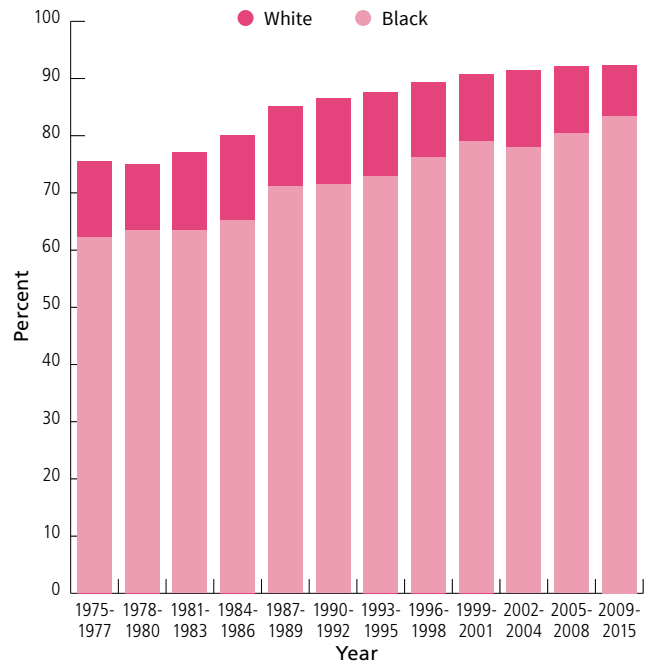
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Race/ethnicity

Five-year relative survival has improved from 76% in 1975-1977 to 92% in 2009-2015 in white women and from 62% to 83% over the same time period in black women (Figure 10). While the racial disparity has narrowed, there remains a substantial gap, especially for late-stage diagnoses (Figure 11).

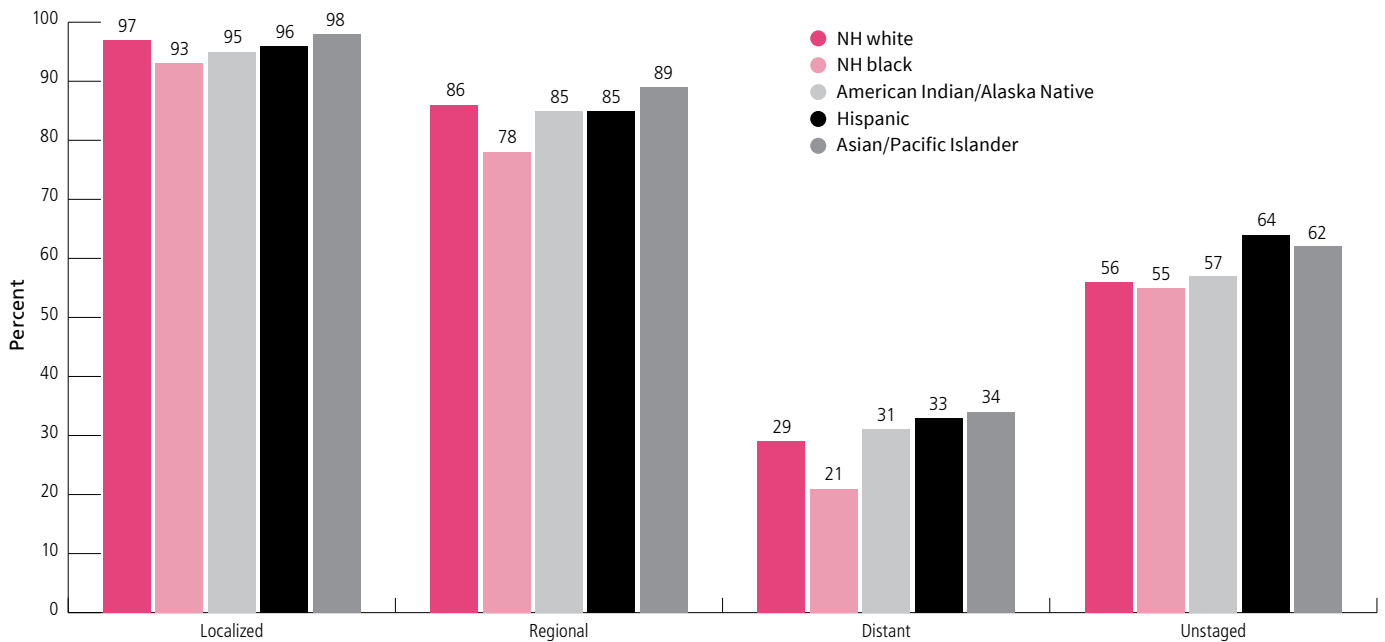
Cause-specific survival instead of relative survival is used to describe the cancer experience of racial and ethnic minorities because reliable life expectancy is not historically available for some groups. Cause-specific survival is the probability of not dying of breast cancer within five years of diagnosis. For every stage at diagnosis, API women have the highest breast cancer survival and NH black women have the lowest (Figure 11). Poverty, less education, and a lack of health insurance are associated with lower breast cancer survival.^{38,39} Of note, high survival rates for API and Hispanic patients are probably overestimated because of incomplete or inaccurate follow-up information in cancer registry data.⁴⁰

Figure 10. Trends in Female Breast Cancer 5-year Relative Survival Rates by Race, US, 1975-2015



Source: SEER Program, 18 SEER registries, National Cancer Institute, 2019.
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Figure 11. Five-year Breast Cancer-specific Survival Rates (%) by Stage at Diagnosis and Race/Ethnicity, US, 2009-2015



Survival rates are based on patients diagnosed during 2009-2015 and followed through 2016.

Source: SEER Program, 18 SEER registries, National Cancer Institute, 2019.

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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 1.2 cases per 100,000 men during 2012-2016.⁴¹ Men are more likely than women (51% versus 36%) to be diagnosed with advanced (regional- or distant-stage) breast cancer,⁸ which likely reflects delayed detection because of decreased awareness.⁴² The death rate for male breast cancer has decreased slightly from 0.4 deaths per 100,000 men during 1975-1979 to 0.3 per 100,000 men during 2013-2017,⁴³ reflecting improvements in treatment.

Due to the infrequency of male breast cancer, much less is known about the disease. Similar to women, male breast cancer risk increases with age. Other risk factors include radiation exposure, *BRCA1/2* gene mutations, family history of breast or ovarian cancer, Klinefelter syndrome, testicular disorders, diabetes, gynecomastia (enlarged breasts), and obesity.^{44,45} In contrast to female breast cancer, studies have found that smoking, alcohol consumption, and physical inactivity are not linked to male breast cancer.^{46,47}

Breast Cancer Risk Factors

The most well-established risk factors for breast cancer are summarized in [Table 4](#). It is estimated that about one-third of postmenopausal breast cancers are linked to potentially modifiable factors, including postmenopausal obesity, physical inactivity, use of combined estrogen and progestin menopausal hormones, alcohol consumption, and not breastfeeding.⁴⁸ Many risk factors (early menarche, late menopause, obesity, and hormone use) affect lifetime exposure of breast tissue to hormones. Hormones are thought to influence breast cancer risk by increasing cell division, 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 early-life exposures during breast development may be particularly critical.⁴⁹ 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.⁵⁰ The following sections present current knowledge about factors associated with breast cancer risk.

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 1.5 times higher for women with one affected first-degree female relative and 2-4 times higher for women with more than one first-degree relative.⁵¹⁻⁵³ Risk is further increased when the affected female relative was diagnosed at a young age or was diagnosed with cancer in both breasts, or if the affected relative is male. 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.⁵¹

A family history of ovarian and perhaps pancreatic or prostate cancer is also associated with increased breast cancer risk.^{54,55} Women should discuss their family history with their health care provider because it may signal the presence of a genetic predisposition to cancer and the need for a different plan for screening and risk reduction.

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

Relative risk	Factor
>4.0	Age (65+ versus <65 years, although risk increases across all ages until age 80) Atypical hyperplasia Lobular carcinoma in situ Pathogenic genetic variations (e.g. <i>BRCA1</i> , <i>BRCA2</i> , <i>PALB2</i> , <i>TP53</i>)
2.1-4.0	Ductal carcinoma in situ High endogenous hormone levels (postmenopausal) High-dose radiation to chest (e.g. Hodgkin lymphoma treatment) Mammographically dense breasts Two or more first-degree relatives with breast cancer
1.1-2.0	Alcohol consumption Early menarche (<11 years) Excess body weight High endogenous estrogen or testosterone levels (premenopausal) Late age at first full-term pregnancy (>30 years) Late menopause (≥55 years) Never breastfed a child No full-term pregnancies One first-degree relative with breast cancer Obesity (postmenopausal) Personal history of ovarian or endometrial cancer Physical inactivity Proliferative breast disease without atypia (usual ductal hyperplasia, fibroadenoma) Recent and long-term use of menopausal hormone therapy containing estrogen and progestin Recent hormonal contraceptive use Weight gain in adulthood Tall height

Note: Relative risks for some factors vary by breast cancer molecular subtype.

Genetic predisposition

Inherited pathogenic (disease-causing) genetic variations in *BRCA1* and *BRCA2*, the most well-studied breast cancer susceptibility genes, account for 5%-10% of all female breast cancers and 15%-20% of all familial breast cancers.^{56,57} These variations are rare (about 1 in 400) 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 1 in 40). Recent studies also document increased frequency of *BRCA* mutations among black and Hispanic breast cancer patients.⁵⁸⁻⁶⁰

Compared to women in the general population who have a 10% risk of developing breast cancer by 80 years of age, risk is estimated to be about 70% in women with pathogenic variants in *BRCA1* and *BRCA2*.⁶¹ The risk of breast cancer by age 70 in women with pathogenic variations in *PALB2*, a different gene that works with *BRCA2*, is estimated to be 35%.⁶² Mutations in other genes are also associated with increased breast cancer risk, including *TP53* (associated with Li-Fraumeni syndrome), *PTEN* (Cowden syndrome), *STK11* (Peutz-Jeghers syndrome), and *CDH1* (associated with diffuse gastric and lobular breast cancer syndrome). In addition, research studies have identified more than 300 more common genetic variants that are associated with slightly elevated risk.⁶³

The US Preventive Services Task Force recommends that primary care providers routinely collect and update family medical history, as well as ancestry. Women with a personal or family history of breast, ovarian, tubal, or peritoneal cancer or those with ancestry associated with *BRCA1/2* gene mutations should be screened with one of several brief questionnaires to determine if there is a need for in-depth genetic counseling to consider genetic testing.⁶⁴ 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, with estimated 10-year risks ranging from 3%-7%.⁶⁵ However, rates of subsequent new breast cancers (also referred to as a new primary breast cancer) have declined steadily since 1985.⁶⁶ The decrease has predominantly been among ER+ breast cancer patients and may reflect the effect of hormonal therapy (e.g., tamoxifen and aromatase inhibitors) and other adjuvant treatments, as well as the rapid increase in breast cancer patients electing bilateral mastectomy for breast cancer treatment (see page 23).^{65,67}

DCIS and LCIS

DCIS is considered a potential precursor to invasive cancer and risk of subsequent breast cancer is greatest at or near the site of DCIS.⁶⁸ Similar to women with a prior

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

Absolute risk is the likelihood of being diagnosed with cancer over a certain period of time. For example, the absolute risk of breast cancer increases with age: 12 out of 10,000 women ages 40-44 versus 23 out of 10,000 women ages 50-54 will be diagnosed with breast cancer in the next year.⁸

Lifetime risk is the absolute risk of being diagnosed with cancer anytime between birth and 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 13% chance of being diagnosed with invasive breast cancer in her lifetime (Table 2). Another way to say this is that 1 out of every 8 women will be diagnosed with breast cancer in her lifetime.

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, meaning they had a 21% increased risk compared to women who have not used hormone therapy.⁶⁹ While relative risks are useful for comparisons, they do not provide information about the absolute risk of the exposed group. In this example, 27 breast cancers per year would be expected to be diagnosed among 10,000 women ages 50-59 who had never used menopausal hormones (their absolute risk) compared to 33 breast cancers among 10,000 women of the same ages who had used estrogen and progestin. Thus, the 21% increased relative risk is the equivalent of 6 additional breast cancers per 10,000 women per year.

invasive breast cancer, women diagnosed with DCIS have a small increased risk for developing a new breast cancer. A recent study estimated that 3%-5% of women diagnosed with DCIS were diagnosed with in situ or invasive breast cancer in the opposite breast within 10 years of their initial diagnosis.⁷⁰

In contrast, LCIS is not generally considered a breast cancer precursor, but is associated with increased risk of developing breast cancer. A recent population-based study of US women diagnosed with LCIS between 1983 and 2014 reported that the 10- and 20-year risk of being diagnosed with DCIS or an invasive breast cancer was 11% and 20%, respectively.⁷¹ Notably, the study also reported that the 20-year breast cancer survival in those diagnosed with DCIS or invasive breast cancer exceeded 95%. Pleomorphic LCIS, a more aggressive subtype, is linked to a higher risk of invasive cancer than classic LCIS and is often treated as though it is a cancer precursor.⁷²

Benign breast disease

Benign breast conditions are categorized 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.⁷³
- 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.⁷³
- Proliferative lesions with atypia are associated with about 4 times higher than average breast cancer risk. These include atypical ductal hyperplasia and atypical lobular hyperplasia.^{73, 74} Recent studies indicate that the 15-year risk of developing in situ or invasive breast cancer exceeds 30% in women diagnosed with atypical hyperplasia.^{74, 75}

Women should keep detailed records of any benign breast biopsy results because they are valuable for risk assessment, screening, and counseling for chemoprevention and other risk-reduction strategies.

Breast density

Breast tissue density is an indicator of the amount of glandular and connective tissue relative to fatty tissue measured during a mammogram and is not determined by how “firm” the breast feels. Following a mammogram, doctors categorize a woman’s breast tissue according to standardized system developed by the American College of Radiology called the Breast Image Reporting and Data System (BI-RADS) as A) fatty; B) scattered areas of fibroglandular tissue; C) heterogeneously dense; and D) extremely dense. Women with breasts classified as C (heterogeneously dense) or D (extremely dense) are referred to as having “dense breasts.” The risk of breast cancer increases with increasing breast density. Women with dense breasts (BI-RADS C or D) have a 1.5- to 2-fold increased risk of breast cancer compared to those with average density (BI-RADS B).⁷⁶ High breast density can also mask the appearance of breast tumors on a mammogram.⁷⁷

Dense breasts are common. About 36% of US women ages 40-74 have heterogeneously dense breasts and about 7% have extremely dense breasts (BI-RADS C or D, respectively).⁷⁸ Breast density is influenced by genetics and other factors. For most women, breast density generally decreases with age, higher body weight, and after pregnancy and menopause.⁷⁹ Some drugs also affect breast density, including tamoxifen (decreases density) and combined menopausal hormone therapy (increases density).^{79,80}

In early 2019, the US Food and Drug Administration proposed a federal rule that mammogram reports include information about breast density. Thirty-eight states and the District of Columbia previously passed some form of breast density legislation. Some state laws require that women with dense breasts be told that they may benefit from supplemental imaging tests, such as ultrasound or MRI. 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.⁸¹ Ongoing clinical trials are evaluating whether digital breast tomosynthesis (DBT) or MRI may be more useful than conventional digital mammography in evaluating dense breasts.⁸² See page 20 for more information on DBT.

Height

Many studies have found that taller women have a higher risk of breast cancer than shorter women.⁸³⁻⁸⁵ A pooled study of more than 5 million women estimated that an increase of 10 cm (about 4 inches) in height was associated with about a 17% higher risk of breast cancer.⁸⁴ Although the reasons are not fully understood, it may reflect differences in early growth as well as hormonal or genetic factors. Height is also associated with a number of other cancers, including colorectal and ovarian cancers.

Menstrual cycles

Breast cancer risk increases with earlier menstruation and later menopause.⁸⁶ For example, breast cancer risk is about 20% higher among those who begin menstruating before age 11 compared to those who begin at age 14 or older. Likewise, women who experience menopause at age 55 or older have about a 12% higher risk compared to those who do so between ages 50-54.⁸⁶ 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.⁵⁰

Bone mineral density

High bone mineral density in postmenopausal women has been associated with a 60%-80% increased risk for breast cancer compared to low bone density; risk appears to be most strongly related to HR+ disease.^{87,88} Bone density is not thought to be an independent risk factor for breast cancer, but a marker of cumulative estrogen exposure.⁸⁹ 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 (e.g., estrogen, progesterone) have about twice the risk of developing breast cancer compared to women with the lowest levels, with the strongest relationships found for HR+ tumors.^{90,91}

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.⁹¹

Although it is challenging to study the relationship of hormones in premenopausal women because levels vary across the menstrual cycle, there is some evidence that high levels of circulating estrogens and androgens are associated with a small excess risk in premenopausal women, particularly for HR+ breast cancer.⁹¹⁻⁹³

Reproductive factors

Pregnancy

Pregnancy has a dual effect on breast cancer risk.⁹⁴ In the short term, women who have had a full-term pregnancy have an increased risk of both HR+ and HR- breast cancers that peaks at 5 years after childbirth. However, after about two decades, the relative risk of HR+ breast cancer becomes slightly lower (by about 20%-25%) in women who have given birth compared to those who have not. Risk is further reduced among women who have their first child at a younger age or have a greater number of children. In contrast, the increased risk for HR- breast cancer persists following a full-term pregnancy.

Fertility drugs

More research is needed on the relationship between breast cancer risk and the long-term effects of ovulation-stimulating drugs.⁹⁵ Most studies to date have found that breast cancer risk is not elevated in women who undergo in vitro fertilization.⁹⁶⁻¹⁰⁰ However, the data are less clear for clomiphene (Clomid), a drug that is often used as a first-line treatment for infertility.^{97,99,100} A long-term follow-up study of women seen at 5 US fertility clinics found no association with ever use of Clomid or gonadotropins; however, risk of invasive breast cancer was increased among women who underwent more than 12 Clomid treatment cycles compared to women who had never used fertility drugs.¹⁰⁰ Another recent study from Norway reported that use of Clomid was linked to a slightly increased risk of breast cancer, but only among women who had given birth.⁹⁹

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. In a review of 47 studies in 30 countries, the risk of breast cancer was reduced by 4% for every 12 months of breastfeeding.¹⁰¹ The protective effect may be stronger for – or even limited to – triple negative cancers.¹⁰²⁻¹⁰⁴

Hormonal birth control

Most studies have found that current or recent use of oral contraceptives (combined estrogen and progesterone) is associated with a small (about 20%) relative increase in breast cancer risk, particularly among women who begin use before first pregnancy.^{105,106} Risk appears to diminish when women stop use, and after about 10 years, it is similar to those who have never taken oral contraceptives. Notably, data are limited and less clear for “ultra low-dose” (20 micrograms) estrogen formulations.¹⁰⁷

Studies of the levonorgestrel-releasing intrauterine device (Mirena) have produced conflicting results, but a large study from Denmark found that use of Mirena also increases breast cancer risk by about 20%.^{105,108-110} In contrast, the use of the injectable progestin-only contraceptive depot-medroxyprogesterone acetate (Depo-Provera) does not seem to be linked with breast cancer.^{105,111} Overall, it has been estimated that one extra breast cancer is diagnosed for every 7,690 women using hormonal contraception for one year.¹⁰⁵

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 HR+ breast cancer, with higher risk associated with longer use.^{50,69,112,113} Risk appears to be greater for women who start hormone therapy soon after the onset of menopause compared to those who begin later.^{113,114} Discontinuation of menopausal hormones diminishes but does not eliminate the increase in breast cancer risk.¹¹⁵ Combined hormone therapy also increases breast density.⁸⁰

Postmenopausal estrogen-only therapy has been associated with uterine problems (including endometrial cancer) and is therefore only given to women who have undergone hysterectomy. The effects of estrogen-only therapy on breast cancer risk is less clear, but they are likely minimal at most. The Women's Health Initiative randomized trial¹¹⁶ found that women who used estrogen-only therapy for an average of 6 years had a 25% lower risk of developing breast cancer, but several 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.^{114, 117, 118} Conflicting results may reflect differences between studies in the prevalence of obesity or higher rates of screening in menopausal hormone users in the observational studies.¹¹⁹

Recently reported results after 18 years of follow-up of the Women's Health Initiative randomized trial found no increased risk of death overall or due to breast cancer associated with use of estrogen plus progestin or estrogen alone.¹²⁰

Excess body weight, physical inactivity, diet, alcohol, and tobacco

Excess body weight and weight gain

Postmenopausal HR+ breast cancer risk is about 1.5-2 times higher in women who are overweight or obese.¹²¹ Even within the normal range of BMI (18.5-24.9), higher levels of body fat are associated with increased risk of breast cancer after menopause.¹²² 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 women with excess body weight.^{122, 123}

Weight gain also increases risk of postmenopausal breast cancer.^{124, 125} A large meta-analysis found that for each 5 kilograms (about 11 pounds) gained during adulthood, risk of postmenopausal breast cancer increases by 11%.¹²⁵ Notably, the increased risk was only observed among women who did not use menopausal hormones. Weight loss in early adulthood and after

menopause is associated with reduced breast cancer risk in some, but not all studies.^{123, 126} The effects of weight loss are more difficult to examine because it is often not sustained.

In contrast, studies have found that excess body weight 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.¹²⁷ The underlying mechanisms for this inverse relationship are not well understood.¹²³

Physical inactivity

Women who get regular physical activity have a 10%-20% lower risk of breast cancer compared to women who are inactive, with greater risk reduction associated with increasing levels of activity.¹²⁸⁻¹³¹ The protective effect is independent of BMI and may be limited to women who have never used menopausal hormone therapy.¹³¹ The benefit may be due to the effects of physical activity on systemic inflammation, hormone levels, and energy balance.^{131, 132}

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. A recent meta-analysis concluded there was no association between breast cancer and dietary fat consumption.¹³³ It has been suggested that soy consumption may reduce breast cancer risk, in part because of historically low breast cancer rates among Asian women, who have a diet high in soy. 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.¹³⁴

There is limited but growing evidence that high levels of fruit and/or vegetable consumption may reduce the risk of HR- breast cancer.¹³⁵⁻¹³⁷ These findings are supported by studies linking lower breast cancer risk to higher

blood levels of carotenoids (micronutrients found in fruits and vegetables).¹³⁸⁻¹⁴⁰ Studies also suggest that calcium-rich diets may be linked to lower risk of breast cancer.¹³⁶ The effect of diet on breast cancer risk remains an active area of research, with studies particularly focused on the 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 10 grams (roughly one drink) of alcohol consumed per day on average.¹⁴¹ Women who have 2-3 alcoholic drinks per day have a 20% higher risk of breast cancer compared to non-drinkers. There is also some evidence that alcohol consumption before first pregnancy may particularly affect risk.^{141, 142} Although mechanisms are not well understood, alcohol may increase risk indirectly by increasing estrogen and other hormone levels.¹⁴³ Alcohol use appears more strongly associated with risk for HR+ than HR- breast cancers.^{50, 144}

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.^{145, 146} A review by American Cancer Society researchers found that women who initiated smoking more than 10 years before the birth of their first child had a 18% higher risk of breast cancer than women who never smoked.¹⁴⁶ Some studies suggest secondhand smoke may increase risk, particularly when exposure happens in childhood and for premenopausal breast cancer.¹⁴⁷⁻¹⁴⁸

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. This may be because breast tissue is most

susceptible to carcinogens before it is fully differentiated, which occurs with first childbirth. Breast cancer risk starts to rise about 8 years after radiation treatment and continues to be elevated for more than 35 years.¹⁴⁹ Although radiation treatments have evolved to include lower doses given over smaller areas, recent studies suggest that the elevated breast cancer risk persists.¹⁵⁰

Diethylstilbestrol (DES) exposure

From the 1940s through 1971, some pregnant women were given the drug 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.¹⁵¹ It remains unclear whether women born to mothers who took DES also have a higher risk.¹⁵¹⁻¹⁵³

Environmental chemicals and pollutants

Many occupational, environmental, and chemical exposures have been proposed as causes of breast cancer. 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 of adults and breast cancer risk,¹⁵⁴ although a recent study found in utero exposure to DDT was linked to elevated breast cancer risk later in life.¹⁵⁵ Animal studies have demonstrated that prolonged, high-dose exposure to many chemicals can increase mammary tumor development, but it is unknown whether the much lower dose exposures that occur in the general environment increase human breast cancer risk. Furthermore, many relevant chemicals have not been adequately studied in humans and this is an active area of research.¹⁵⁶⁻¹⁵⁸

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.^{159, 160} Elevated risk appears to be most strongly associated with shift working during early

adulthood.^{161, 162} 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.¹⁶³ Based on the results of studies in humans and animals, the International Agency for Research on Cancer has concluded that shift work, particularly at night, is probably carcinogenic to humans.¹⁶⁴

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.¹⁶⁵ 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).¹⁶⁶

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.¹⁶⁷

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.¹⁶⁸ In addition, breast implants can obstruct the view of breast tissue during mammography. Women 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.

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 has approved two drugs to help lower the risk of breast cancer in high-risk women: tamoxifen and raloxifene (postmenopausal women only). These drugs are classified as selective estrogen receptor modulators (SERMs) because they block estrogen in some tissues of the body, but act like estrogen in others.

A large meta-analysis, including more than 83,000 high-risk women, found that SERMs reduced breast cancer risk by 38% over 10 years.¹⁶⁹ Although the benefit is limited to ER+ disease, these drugs lower the risk of both invasive cancer and DCIS. 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.¹⁶⁹

Clinical trials have shown that another class of drugs – aromatase inhibitors – also reduce breast cancer risk (by more than half) among high-risk postmenopausal women.¹⁷⁰ As a result, the US Preventive Services Task Force recently expanded their recommendations to include aromatase inhibitors, as well as SERMs, for breast cancer risk reduction in high-risk women.¹⁷¹ Aromatase inhibitors can decrease bone density, so women taking these drugs must be monitored for osteoporosis.

Prophylactic surgery

Women at very high risk of breast cancer (such as those with pathogenic *BRCA* gene variants) may elect prophylactic (preventive) mastectomy. Removal of both breasts reduces the risk of breast cancer by 90% or more.¹⁷² Prophylactic salpingo-oophorectomy (surgical removal of the fallopian tubes and ovaries) reduces the risk of ovarian cancer, but the benefit for breast cancer in high-risk women is less clear and may be limited to

BRCA2 mutation carriers.¹⁷³ Importantly, however, many women who elect prophylactic surgery would not have developed cancer. Women considering these options should discuss the benefits and limitations with their

doctor, and a second opinion is strongly recommended. See page 23 for further discussion of contralateral prophylactic mastectomy in women diagnosed with unilateral breast cancer.

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. The recommendations for average-risk women were most recently updated in 2015 (see box, opposite page);¹⁷⁴ recommendations for women at increased risk will be updated in 2020.

Mammography

Mammography is a low-dose x-ray image of breast tissue. Although early mammographic images were on x-ray film, digital technology, in which a 2-dimensional (2D) image of breast tissue is captured electronically and viewed on a monitor, has largely replaced screen-film mammography. Digital mammography has improved sensitivity for women under age 50 and those with dense breast tissue.¹⁷⁵

Early detection of breast cancer by mammography reduces the risk of breast cancer death and increases treatment options, including less extensive surgery and/or the use of chemotherapy with fewer side effects, and sometimes, the option to forgo chemotherapy. Combined analysis of breast cancer screening in randomized trials has demonstrated an overall reduction in breast cancer deaths of about 20%.¹⁷⁶ More recent results from organized mammography programs in Europe and Canada indicate that the risk of breast cancer death was reduced by more than 40% among women who were screened.¹⁷⁷⁻¹⁷⁹

Women should also be informed of the limitations of mammography. Mammography will not detect all breast cancers, and some breast cancers detected by screening still have poor prognosis. Mammography screening may also lead to overdiagnosis. That is, some breast tumors or

lesions detected by mammography, particularly DCIS, would not have progressed or otherwise been detected without screening. Estimates of the prevalence of overdiagnosis vary widely because it cannot be directly measured.¹⁸⁰ Mammography may also result in false-positive results, which lead to follow-up examinations, including biopsies, when there is no cancer; false positives are more likely when women have their first screening. About 12% of women screened with modern digital mammography require follow-up imaging or biopsy, but most (95%) of these women do not have cancer.¹⁸¹ Cumulative radiation exposure from repeated mammograms may slightly increase the risk of breast cancer;¹⁸² however, the dose of radiation during a mammogram is relatively small and the benefit of screening likely outweighs any harm. Reducing radiation exposure through more effective imaging is an area of current research.

The Affordable Care Act requires that Medicare and all new private health insurance plans fully cover screening mammograms without any out-of-pocket expense for patients. There are also programs, such as the CDC's National Breast and Cervical Cancer Early Detection Program, that offer mammography services for low-income, uninsured, and underserved women. For help locating a free or low-cost screening mammogram in your area, contact the American Cancer Society at 1-800-227-2345.

Digital breast tomosynthesis (DBT)

In 2011, the FDA approved the use of DBT (also referred to as 3D mammography) for breast cancer screening. DBT takes multiple breast images, in combination with digital 2D mammography, which can be used to construct a 3D image of the breast. Some studies have found that DBT may be more sensitive (i.e., detect more cancers) and have

American Cancer Society Guideline for Breast Cancer Screening, 2015¹⁷⁴

The recommendations below are for women at average risk of breast cancer (i.e., women without a personal history of breast cancer, a suspected or confirmed pathogenic genetic variation [e.g., *BRCA1* or *BRCA2*], a strong family history, or a history of previous radiotherapy to the chest at a young age). All women should become familiar with the potential benefits, limitations, and harms associated with breast cancer screening.

- Women should have the opportunity to begin annual screening between the ages of 40 and 44.
- Women ages 45 to 54 should be screened annually.
- Women ages 55 and older should transition to biennial screening or have the opportunity to continue screening annually.
- Women should continue screening mammography as long as their overall health is good and they have a life expectancy of 10 years or more.

lower recall rates than 2D mammography alone,^{183, 184} however, when 2D images are produced separately from DBT, women receive about twice the dose of radiation. The FDA has approved the use of tomographic images to produce synthetic 2D images, which reduces the radiation dose levels similar to conventional digital mammography, although this practice is not yet widespread. DBT is not yet available in all communities and may not be fully covered by health insurance.

Prevalence of mammography

- In 2018, the prevalence of up-to-date mammography according to American Cancer Society recommendations was lower among Hispanic and Asian (55%-60%) women than NH black (66%), NH white, and AIAN (both 64%) women (Table 5).¹⁸⁵ However, studies have documented that self-reported survey data overestimate mammography screening prevalence, particularly among black and Hispanic women.^{34- 36, 186}

Table 5. Mammography (%), Women 45 and Older, US, 2018

	Up to date* (≥ 45 years)	Within the past 2 years (50-74 years)
Overall	63	73
Age (years)		
45-54	53	–
55-64	73	–
65-74	75	75
75+	51	–
Race/Ethnicity		
Non-Hispanic White	64	73
Non-Hispanic Black	66	74
Non-Hispanic Asian American	55	71
Non-Hispanic American Indian and Alaska Native	64	66
Hispanic	60	71
Sexual orientation		
Gay/Lesbian	70	79
Straight	63	73
Bisexual	†	†
Education		
Less than high school	52	63
High school diploma or GED	61	69
Some college/associates degree	64	72
College graduate	70	81
Health insurance status (age ≤64 years)		
Uninsured	30	39
Insured	64	75
Immigration		
Born in US	64	73
Born in US territory	68	†
In US fewer than 10 years	43	54
In US 10 or more years	61	74

GED = General Educational Development high school equivalency. *According to American Cancer Society recommendations: mammogram within the past year (ages 45-54 years) or past two years (ages ≥55 years). †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, 2018.

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- Only 30% of uninsured women were up to date with breast cancer screening in 2018, compared to 64% of insured women.
- The prevalence of up-to-date breast cancer screening was 70% or higher among lesbian women, college graduates, and those ages 55-74 years.
- In 2016, by state, the prevalence of up-to-date mammography among women ages 45 and older ranged from 57% in Wyoming to 79% in Rhode Island (Table 6).¹⁸⁷

Table 6. Mammography (%) by State, Women 45 and Older, 2016

	Up to date* (≥ 45 years)	Within the past 2 years (50-74 years)
Alabama	72	78
Alaska	58	68
Arizona	66	76
Arkansas	65	73
California	71	82
Colorado	64	74
Connecticut	77	86
Delaware	76	82
District of Columbia	72	84
Florida	75	82
Georgia	72	79
Hawaii	74	84
Idaho	58	64
Illinois	69	78
Indiana	64	72
Iowa	71	78
Kansas	68	75
Kentucky	71	77
Louisiana	70	78
Maine	73	81
Maryland	74	81
Massachusetts	78	86
Michigan	71	79
Minnesota	73	82
Mississippi	65	72
Missouri	69	76
Montana	66	74
Nebraska	64	73
Nevada	62	73
New Hampshire	73	82
New Jersey	73	81
New Mexico	60	72
New York	70	80
North Carolina	72	79
North Dakota	69	75
Ohio	70	77
Oklahoma	66	74
Oregon	66	74
Pennsylvania	68	76
Rhode Island	79	85
South Carolina	68	76
South Dakota	72	79
Tennessee	68	77
Texas	64	73
Utah	65	77
Vermont	70	79
Virginia	73	80
Washington	66	76
West Virginia	71	78
Wisconsin	72	80
Wyoming	57	64
United States (median)	70	78

*According to American Cancer Society recommendations: mammogram within the past year (ages 45-54 years) or past two years (ages ≥55 years).
Note: Mammography prevalence estimates do not distinguish between examinations for screening and diagnosis.

Source: Behavioral Risk Factor Surveillance System, 2016.

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Magnetic resonance imaging (MRI)

Breast MRI uses high-powered magnets along with radio waves and computers to produce an image. In 2007, the American Cancer Society published recommendations for the use of MRI for screening women at increased risk of breast cancer.¹⁸⁸

Beginning at age 30, annual screening with MRI, in addition to mammography, is recommended for women with an estimated lifetime risk of breast cancer of at least 20%-25% due to the presence of a high-risk variation in the breast cancer susceptibility genes *BRCA1* or *BRCA2*, a first-degree relative with a *BRCA1* or *BRCA2* mutation (if the woman herself has not been tested), a strong family history of breast and/or ovarian cancer, prior chest radiation therapy (e.g., for Hodgkin lymphoma), as well as women with Li-Fraumeni, Cowden, and Bannayan-Riley-Ruvalcaba syndromes and their first-degree relatives.¹⁸⁸

Women with an estimated 15%-20% lifetime risk, including women with dense breast tissue, should talk with their doctors about the benefits and limitations of adding MRI screening to their annual mammogram. MRI screening is not recommended for women whose lifetime risk of breast cancer is less than 15%. Studies indicate that MRI is underutilized among high-risk women and overutilized by women who are not at high risk for breast cancer.¹⁸⁹ MRI should supplement not replace mammography and should be done at facilities that are accredited by the American College of Radiology. Although MRI is more expensive than mammography, most major insurance companies will cover some portion of the cost if a woman is demonstrated to be at sufficiently high risk.

Breast ultrasound

Breast ultrasound is sometimes used to evaluate abnormal findings from a mammogram or physical exam. It is completed with a wand-like handheld device that captures images of the breast with sound waves. For women with mammographically dense breast tissue, ultrasound combined with mammography may be more sensitive than mammography alone; however, it also increases the likelihood of false-positive results.^{190, 191} 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 breast cancer screening in average-risk asymptomatic women based on lack of clear benefits for CBE alone or in conjunction with mammography.¹⁷⁴ Furthermore, there is some evidence that adding CBE to mammography screening increases the rate of false positives.

Breast self-awareness

Although the American Cancer Society also no longer recommends that women perform monthly breast self-exams (BSE), all women should become familiar with both the appearance and feel of their breasts and report any changes promptly to their physician. If a lump or other symptoms develop, women should contact a doctor immediately, even after a recent normal mammogram.

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.

Ductal carcinoma in situ

Since there is currently no certain way to determine the progressive potential of a DCIS lesion, surgery and sometimes radiation and/or hormonal therapy are the usual course of action following a diagnosis of DCIS. However, there is likely a group of patients that could safely forgo surgical treatment for DCIS.¹⁹² Several clinical trials are currently underway that are comparing standard treatment to active monitoring (with optional hormonal therapy) in women with "low-risk" DCIS.⁶ Ongoing research also seeks to identify molecular markers of DCIS that could predict recurrence or progression to invasive cancer.

Invasive breast cancer

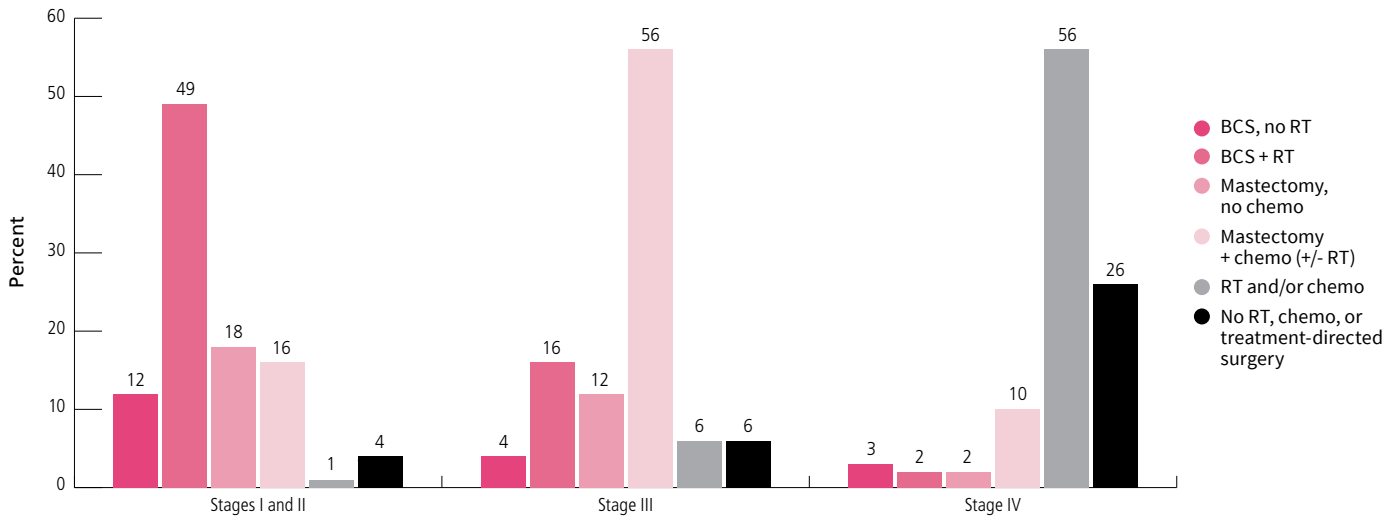
Figure 12 shows treatment patterns among US women with invasive breast cancer in 2016 by stage at diagnosis. Most women with early-stage breast cancer will have some type of surgery, which is often combined with other treatments such as radiation therapy, chemotherapy, hormone therapy, and/or targeted therapy to reduce the risk of recurrence. Patients with metastatic disease are primarily treated with systemic therapies, which can include chemotherapy, targeted therapy, hormonal therapy, and more recently immunotherapy.

Surgery

The primary goals of breast cancer surgery are to remove the cancer and determine its stage. Surgical treatment involves mastectomy (surgical removal of the entire breast) or breast-conserving surgery (BCS). 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 high tumor-to-breast ratio, multiple tumors within the same breast, or inflammatory or locally advanced cancers. In most cases, BCS is followed by radiation to the breast. Mastectomy can also be followed by radiation.

Despite equivalent survival when combined with radiation, BCS-eligible patients are increasingly electing mastectomy for a variety of reasons, including reluctance to undergo radiation therapy, fear of recurrence, and desire for symmetry.^{193, 194} Some women who are diagnosed with breast cancer in one breast also choose to have the unaffected breast removed, which is known as bilateral mastectomy or contralateral prophylactic mastectomy (CPM). Younger patients (<40 years of age) and those with larger and/or more aggressive tumors are more likely to be treated with mastectomy or CPM.¹⁹⁵⁻¹⁹⁷ Although CPM nearly eliminates the risk of developing a new breast cancer, it does not improve long-term breast cancer survival for the majority of women and nearly doubles the risk of surgical complications.¹⁹⁸⁻²⁰⁰ In the US, the percentage of surgically treated women with early-stage disease in one breast who undergo CPM has increased rapidly, from 10% in 2004 to 33% in 2012 among women ages 20-44 and from 4% to 10% among those 45 years of age and older.¹⁹⁷

Figure 12. Female Breast Cancer Treatment Patterns (%), by Stage, US, 2016



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

Source: National Cancer Data Base, 2016 as provided in *Cancer Treatment & Survivorship Facts & Figures 2019-2021*.

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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. 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.

Both BCS and mastectomy are usually accompanied by removal of one or a few regional lymph nodes from the armpit (axilla) to determine if the disease has spread beyond the breast. This procedure identifies the lymph node(s) to which cancer is most likely to spread and is called sentinel lymph node biopsy (SLNB). The presence of cancer cells in the lymph nodes increases the risk of recurrence, and so results from the SLNB can help determine whether further treatment is needed. Some breast cancer patients need to undergo more extensive lymph node surgery, called an axillary lymph node dissection (ALND). Surgery 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.²⁰¹ Axillary radiation and excess body weight are also associated with increased risk of lymphedema. The onset of symptoms usually occurs within 3 years of surgery, but has been reported to occur

even 20 or more years later.²⁰² Early diagnosis and treatment are critical to reduce the risk of progression to more severe lymphedema.

For more information about breast cancer survivorship, see *Cancer Treatment and Survivorship Facts & Figures*, available online at [cancer.org/statistics](https://www.cancer.org/statistics).

Radiation therapy

Radiation therapy is often used after surgery to destroy cancer cells remaining in the breast, chest wall, or underarm area and reduce the risk of recurrence. 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.²⁰³ However, studies have shown that radiation does not improve survival for breast cancer patients 70 years of age and older with small, lymph node-negative, HR+ cancers who take hormonal therapy, although it does reduce the risk of local recurrence.²⁰⁴ Older patients with HR+ tumors who opt to omit radiation must be aware of the heightened importance of adhering to their prescribed hormonal therapy regimen. Some mastectomy-treated patients also benefit from radiation if their tumor is larger than 5 centimeters, growing into 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, internal radiation therapy (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 preferences. 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. 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. Accumulating evidence suggests that radiation therapy given at higher doses over fewer days (known as accelerated partial breast irradiation) may be as effective as conventional therapy.²⁰⁵ Intra-operative radiation therapy, in which a single fraction of radiation is given into the cavity left by tumor removal during BCS, is also sometimes an option.

Systemic therapy

Systemic therapies are drugs that travel through the bloodstream, potentially affecting all parts of the body, and work using different mechanisms. For example, chemotherapy drugs generally attack cells that grow quickly. Hormonal therapy works by either blocking or decreasing the level of the body's natural hormones, which sometimes act to promote cancer growth. Targeted therapies work by attacking specific proteins on cancer cells (or nearby cells) that normally help them grow. Immunotherapy stimulates the patient's immune system to attack the cancer.

When systemic therapy 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). Systemic treatment given to patients after surgery is called adjuvant therapy and 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.

Systemic therapy can affect fertility in premenopausal women, so young breast cancer patients who are interested in future childbearing should consult with a reproductive endocrinologist to determine fertility prevention strategies. In addition, hormonal therapy is not recommended during pregnancy and chemotherapy can cause premature ovarian failure.

Chemotherapy

The benefit of chemotherapy is dependent on multiple factors, including the size of the tumor and the number of lymph nodes involved, as well as HR and HER2 status. Triple negative and HER2+ breast cancers tend to be more sensitive to chemotherapy than HR+ tumors.²⁰⁶ There are also gene expression panels (such as Oncotype DX, PAM 50, and MammaPrint) that can help assess the risk of distant recurrence and potentially identify those who would more likely benefit from adjuvant chemotherapy. The Oncotype Dx 21-Gene Recurrence Score is used most widely in the United States, but it is only applicable for patients with early-stage HR+/HER2- breast cancer. A high recurrence score identifies women who will benefit from adjuvant chemotherapy (in addition to hormonal therapy), whereas a low score identifies women who could safely avoid it. Evidence is less clear for patients with intermediate risk scores, although recent clinical trial results based on 9 years of follow-up suggest that most patients over age 50 with intermediate scores are unlikely to benefit from the addition of chemotherapy.²⁰⁷

Although most women who are treated with chemotherapy receive it after surgery, a recent study documents an increase in the use of neoadjuvant chemotherapy, particularly among patients with HER2+ and triple negative breast cancers.²⁰⁸ A summary analysis of clinical trials recently concluded that neoadjuvant chemotherapy is as effective as the same therapy given after surgery in terms of survival and distant recurrence.²⁰⁹ However, breast and axillary surgery remains necessary after neoadjuvant chemotherapy, even when the preoperative treatment appears to have completely

cleared all clinical evidence of the cancer. Recent clinical trials have focused on identifying therapies that can improve outcomes among neoadjuvantly treated breast cancer patients who have residual disease detected during surgery.^{210, 211}

Hormonal (endocrine) therapy

Estrogen, a hormone produced by the ovaries in addition to other tissues, promotes the growth of HR+ breast cancers. About 83% of breast cancers are HR+ (Figure 1) and can be treated with hormonal therapy to 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.

For premenopausal women, tamoxifen for up to 10 years is standard treatment; however, the combination of ovarian suppression and either tamoxifen or an aromatase inhibitor is recommended for those women with a high risk of recurrence.²¹² For postmenopausal women, aromatase inhibitors (i.e., letrozole, anastrozole, and exemestane) are the preferred hormonal treatment. The decision to treat with an aromatase inhibitor beyond 5 years is individualized based on patient factors and the expected benefit from the reduction in risk of subsequent breast cancers. Studies have found that adherence to hormonal therapies remains suboptimal, particularly among black women, and may be in part due to out-of-pocket costs.^{213, 214}

Targeted therapy

Multiple medications are available for the treatment of the HER2+ subtype, which accounts for about 15% of all female breast cancers in the US (Figure 1). Trastuzumab, the first approved drug, is a monoclonal antibody that directly targets the HER2 protein. Several newer drugs have been developed that target the HER2 protein and can be used in combination with trastuzumab or if trastuzumab is no longer working. All invasive breast cancers should be tested for HER2 to identify women who would benefit from this therapy. Additional targeted therapy drugs, such as CDK4/6, PARP, and PIK3 inhibitors, are available for treatment of select patients with advanced disease.

Immunotherapy

Immunotherapy drugs are an emerging area of breast cancer treatment. These drugs stimulate a person's own immune system to recognize and destroy cancer cells more effectively. Checkpoint inhibitors are one type of immunotherapy drug that has been identified to treat some breast cancers, particularly the triple negative subtype. Drugs that target these checkpoints help to restore the immune response against breast cancer cells. Atezolizumab targets the PD-L1 "checkpoint" and can be used along with the chemotherapy drug nab-paclitaxel in patients with advanced triple negative breast cancer whose tumor makes the PD-L1 protein.²¹⁵ Research on other immunotherapy drugs for metastatic breast cancer treatment is ongoing.

What Is the American Cancer Society Doing about Breast Cancer?

With a dedicated team of volunteers and staff, the American Cancer Society is leading the fight for a world without breast cancer – and all cancers.

Patient and caregiver services

The American Cancer Society provides patients and caregivers with resources that can help improve – and

even save – lives. From free rides to treatment and other cancer-related appointments, places to stay when treatment is far from home and our 24/7 helpline, we're here for everyone with cancer questions and concerns, when and where they need us.

Cancer information

Caring, trained American Cancer Society staff connect people to answers about a breast cancer diagnosis, health insurance assistance, American Cancer Society programs and services, and referrals to other services at our 24/7 helpline at 1-800-227-2345. Our website, [cancer.org](https://www.cancer.org), offers reliable and accurate breast cancer information and news, including current information on treatments and side effects, and programs and services nearby. We also help people who speak languages other than English or Spanish find the assistance they need at [cancer.org/easyreading](https://www.cancer.org/easyreading) or [cancer.org/cancer-information-in-other-languages](https://www.cancer.org/cancer-information-in-other-languages).

People can visit [cancer.org/breastcancer](https://www.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](https://www.cancer.org/bookstore) for a complete list of books that are available for order. All of our books are also available from all major book retailers such as Amazon and Barnes & Noble. Call 1-800-227-2345 or visit [cancer.org](https://www.cancer.org) for brochures.

Programs and services

Survivorship: American Cancer Society survivorship work aims to help people living with and beyond cancer from diagnosis through long-term survivorship to the end of life. Efforts focus on helping survivors understand and access treatment; manage their ongoing physical, psychosocial, and functional problems; and engage in healthy behaviors to optimize their wellness. Our posttreatment survivorship care guidelines are designed to promote survivor healthiness and quality of life by facilitating the delivery of high-quality, comprehensive, coordinated clinical follow-up care. Our survivorship research efforts focus on understanding the impact of cancer on multiple facets of survivors' lives and on developing and testing interventions to help survivors actively engage in their health care and improve their health and well-being through and beyond treatment. Through the National Cancer Survivorship Resource Center, a collaboration between the American Cancer Society and the George Washington University Cancer

funded by the Centers for Disease Control and Prevention, we created the Cancer Survivorship E-Learning Series for Primary Care Providers. The free e-learning program is designed to teach clinicians how to care for survivors of adult-onset cancers.

Support for caregivers: Approximately 7% of the US population is made up of family caregivers of a loved one with cancer, and we are committed to meeting their information, education, and support needs. Approximately 4% of the US population is surviving cancer, meaning the ratio of family caregivers to cancer survivors is nearly double, supporting the notion that cancer is not isolated only to the individual diagnosed but rather impacts an entire family unit and network of close friends. One of the informational tools we offer caregivers is our *Caregiver Resource Guide*, which can help them: learn to care for themselves as a caregiver, better understand what their loved one is going through, develop skills for coping and caring, and take steps to help protect their own health and well-being.

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. It has specially trained patient navigators across the country who can help: find transportation to treatment and other 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.

Breast cancer support

The American Cancer Society Reach To Recovery® program connects trained volunteers with breast cancer patients to provide peer-to-peer support on everything from practical and emotional issues to helping them cope with their disease, treatment, and long-term survivorship issues.

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 and caregivers can find others with similar experiences and interests. At [csn.cancer.org](https://www.csn.cancer.org), members can participate on discussion boards, join the chat room, and build their own support network from among other members. Other online resources, including Springboard Beyond Cancer and Belong, provide additional support for patients, survivors, and caregivers and allow them to better communicate to receive the help they need during and after cancer.

Transportation to treatment

Lack of transportation can be one of the biggest roadblocks to treatment. That is why the American Cancer Society started the Road To Recovery® program. It is at the very heart of our work of removing barriers to quality health care by providing patients transportation to treatment through volunteer drivers, partners, or community organizations. Other transportation programs are also available in certain areas.

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 that helps patients access the care they need. Through our Hotel Partners Program, we also partner with local hotels across the country to provide free or discounted lodging for patients and their caregivers who are not able to make frequent trips for treatment appointments.

Hair-loss and mastectomy products

The American Cancer Society “tlc” *Tender Loving Care*® publication offers affordable hair loss and mastectomy products for women coping with cancer, as well as advice on how to use those products. Products include wigs, hairpieces, hats, turbans and breast forms, as well as mastectomy bras, camisoles, and swimwear. Call 1-800-850-9445, or visit the “tlc”™ website at [tlcdirect.org](https://www.tlcdirect.org) to order products or catalogs.

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](https://www.cancer.org/survivorshipguide) to download a free copy of the guide.

The American Cancer Society also has 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.²¹⁶ 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

Research is at the heart of the American Cancer Society’s mission. We invest 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. Ongoing research studies span the cancer continuum from prevention and early detection to treatment and beyond. As of August 1, 2019, the American Cancer Society is funding more than \$67 million in breast cancer research through 162 research and training grants.

Examples of projects in which researchers in the American Cancer Society Extramural Research program are engaged include:

- Identifying new targets for treating triple negative breast cancers
- Understanding the role of the immune system in the spread of breast cancer to other parts of the body

- Evaluating the effects of a high-protein, low-calorie diet on breast tissue and the risk of breast cancer recurrence
- Examining the impact of breast density legislation on women's breast cancer knowledge and screening decisions

Internally, the American Cancer Society also conducts epidemiologic studies of breast cancer and performs surveillance and health services research to understand the factors that underlie racial and socioeconomic disparities in breast cancer screening, incidence, treatment, survival, and mortality. Using information collected from more than 600,000 women in Cancer Prevention Study-II, American Cancer Society epidemiologists study the influence of many risk factors, including alcohol consumption, physical activity, menopausal hormones, 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. When female participants are diagnosed with breast cancer, consent is requested to bank tumor tissue specimens to better understand differences in risk and prognostic factors by molecular subtypes of breast cancer. The blood and tissue specimens together with the 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; to increase government funding for breast cancer research; and to 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. Women who are uninsured are much less likely to be screened for cervical and breast cancer than those who are insured. The NBCCEDP program helps to decrease this disparity in screening. Unfortunately, only one in 10 eligible women can be served by the program due to lack of federal and state funding. ACS CAN is asking Congress and states 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. Additionally, states have considered proposals that could jeopardize access to this program through the 1115 demonstration waiver process.

Breast Density and Mammography Reporting:

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 Food and Drug Administration proposed a rule to incorporate breast density reporting on mammograph reports for the first time. ACS CAN has advocated for several years for a national standard developed through an evidence-based process to inform women about breast density and risk.

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 June 1, 2019, 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 publication refer to invasive (not in situ) female breast cancer.

Estimated new breast cancer cases. The overall estimated number of new invasive breast cancer cases diagnosed in the US in 2019 was projected using a spatiotemporal model based on incidence data from 48 states and the District of Columbia for the years 2001-2015 that met the North American Association of Central Cancer Registries' (NAACCR) data inclusion standards.⁸ 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. The number of DCIS cases diagnosed in 2019 were estimated by 1) approximating the actual number of cases in the 10 most recent data years (2007-2016) by applying annual age-specific incidence rates (based on 48 states) to corresponding population estimates for the

overall US; 2) calculating the average annual percent change (AAPC) in cases over this time period; and 3) using the AAPC to project the number of cases three years ahead. These estimates were also partially adjusted for expected reporting delays using invasive factors. The estimated number of DCIS invasive cases by age and overall were calculated as the proportions of cases in each age group in the NAACCR data during 2012-2016 applied to the overall 2019 DCIS and invasive estimates.

Incidence rates. Incidence rates are defined as the number of people who are diagnosed with cancer divided by the number of people who are at risk for the disease in the population during a given time period. Incidence rates in this publication are presented per 100,000 people per year and are age adjusted to the 2000 US standard population. Breast cancer incidence rates for the US in the most recent time period (2012-2016) were calculated using data on cancer cases collected by NAACCR.⁸ When referenced as such, NAACCR incidence data were made

available on the NAACCR website (naaccr.org) and within the Cancer in North America publications.^{217,218} Long-term (1975-2016) incidence trends are based on the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) 9 registries, which account for about 8% of the US population. Analyses of trends (2001-2016) by race/ethnicity are based on NAACCR incidence data and were adjusted for reporting delay using delay factors for the SEER 21 registries.

Breast cancer subtype distribution. Using the approach of Anderson et al,²¹⁹ we imputed missing estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2) status assuming that status was missing at random, conditional on year of diagnosis, age, race/ethnicity, and ER/PR/HER2 status. Specifically, two-step imputation was performed to obtain imputed HR status based on the joint distribution of ER (positive, negative, and missing) and PR (positive, negative, and missing) status. Please see DeSantis et al³⁷ for more information on this method.

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 2002-2016 to a statistical model that forecasts the number of deaths expected to occur in 2019. Data on the number of deaths are obtained from the National Center for Health Statistics (NCHS) at the Centers for Disease Control and Prevention (CDC). Age-specific estimates were calculated using the proportions of deaths that occurred in each age group during 2013-2017 applied to the overall 2019 estimate.

Mortality rates. Similar to incidence rates, mortality rates (or death rates) are defined as the number of people who die from cancer divided by the number of people at risk in the population during a given time period. 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 2009-2015; 10-year survival rates are based on diagnoses during 2001-2015; and 15-year survival rates are based on diagnoses during 1998-2015. All patients were followed through 2016. When referenced as such, 5-year survival statistics were originally published in SEER Cancer Statistics Review, 1975-2016.²⁰

Probability of breast cancer diagnosis or death.

Probabilities of developing or dying from breast cancer were calculated using DevCan 6.7.7 (Probability of Developing Cancer Software), developed by the National Cancer Institute.²²⁰ These probabilities reflect the average experience of women in the US who were not previously diagnosed with breast cancer and do not take into account individual behaviors and risk factors (e.g., utilization of mammography screening and family history of breast cancer).

Screening. State-level prevalence estimates of mammography are based on Behavioral Risk Factor Surveillance System (BRFSS) data.¹⁸⁷ The BRFSS is an ongoing system of surveys conducted by the state health departments in cooperation with the CDC. Data from the CDC's National Health Interview Survey were used to generate national prevalence estimates of mammography.¹⁸⁵

Important note about estimated cases and deaths.

While these estimates provide a reasonably accurate portrayal of the current cancer burden in the absence of actual data, they should be interpreted with caution because they are model-based projections that may vary from year to year for reasons other than changes in cancer occurrence. In addition, they are not informative for tracking cancer trends. Instead, trends in cancer occurrence should be analyzed using age-adjusted incidence rates reported by population-based cancer registries and mortality rates reported by the NCHS.

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For more information, contact:

Carol DeSantis; Rebecca Siegel; Ahmedin Jemal
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