



## Use of endocrine therapy following diagnosis of ductal carcinoma in situ or early invasive breast cancer

# Use of Endocrine Therapy

## Data Points # 14

In 2012, approximately 230,000 women in the United States were diagnosed with invasive breast cancer. In addition, about 60,000 women were diagnosed with ductal carcinoma in situ (DCIS), a possible risk factor for invasive breast cancer.<sup>1</sup> Most breast cancers (about 75%) contain significant numbers of estrogen receptors (this is called estrogen receptor positive or ER+).<sup>2</sup> In these cases, tumor growth is stimulated by the presence of estrogen.

Two types of endocrine medications treat ER+ DCIS and early invasive breast cancer: tamoxifen and aromatase inhibitors (AIs).<sup>3</sup> Both act by reducing the amount of estrogen that reaches the tumor. Tamoxifen is a selective ER modulator that prevents estrogen from binding to the receptors. In contrast, AIs block the synthesis of estrogens. Currently, three AIs are on the market: anastrozole, letrozole, and exemestane. Both tamoxifen and AIs have been shown in randomized trials to reduce the risk of breast cancer recurrence and the development of a new primary tumor in the contralateral (opposite) breast.<sup>3-5</sup>

Treatment of DCIS and early invasive breast cancer, regardless of ER status, includes mastectomy or breast-conserving surgery (BCS) (recommended in conjunction with radiation therapy [RT] or mastectomy).<sup>3</sup> In addition, guidelines from the National Comprehensive Cancer Network (NCCN) recommend endocrine treatment with tamoxifen or AIs for at least five years for women with ER+ invasive breast cancer.<sup>3,6</sup> Current NCCN guidelines recommend that physicians consider tamoxifen treatment for five years for patients with DCIS, especially those with ER+ disease; however, NCCN guidelines do not specifically recommend treatment with AIs.<sup>3,6</sup>

Studies of adherence to AIs and tamoxifen find that up to one-third of women discontinue use within three years of starting.<sup>7</sup> Adverse effects are the most common reason for discontinuation. Tamoxifen use is associated with more hot flashes and with gynecologic problems such as uterine cancer.

Women with ductal carcinoma in situ (DCIS) were more likely to be treated with tamoxifen than an aromatase inhibitor (AI). For women with early invasive breast cancer, the reverse pattern was seen, with AI use more common than tamoxifen use.

Use of endocrine therapy declined in the five years following diagnosis for both DCIS and early invasive breast cancer. At all time points, use was higher for early invasive breast cancer, but declines were also greater.

Endocrine therapy use was associated with similar demographic characteristics for DCIS and early invasive breast cancer. In both groups, use declined with age.

Tumor characteristics were more strongly related to therapy use for women with early invasive disease than DCIS. With early invasive disease, use increased with increasing tumor size and declined with higher grade. For DCIS, patterns across both factors were less clear.

Endocrine therapy use was highest for women with DCIS treated with breast-conserving surgery plus radiation therapy (BCS+RT) compared with either mastectomy or BCS alone. For women with early invasive cancers, therapy was highest for women treated with BCS+RT and lowest for women treated with BCS alone.



AI use is associated with increased cardiovascular disease, bone loss, and painful joints. Both drugs seem to have similar adherence problems despite distinct adverse effect profiles.<sup>7,8</sup> Prior to the passage of the Medicare Part D benefit, the Medicare program provided no coverage for tamoxifen or AIs; however, both classes of medication are now included in Part D benefits. Thus, beginning in 2007, it is possible to examine use of these medications among elderly patients enrolled in Medicare Part D.

In this report, we sought to quantify the use of tamoxifen and AIs in 2007 and 2008 among older women within five years of diagnosis with DCIS or early invasive breast cancer (i.e., those diagnosed between 2002 and 2007; see **Figure 1**).

## METHODS

We identified women diagnosed with DCIS and early invasive breast cancer (i.e., stage 1 cancer) in the Surveillance, Epidemiology, and End Results (SEER)-Medicare data linkage between December 2002 and December 2007. We limited the sample to women age 65 and older at diagnosis, who were enrolled in Medicare Part D for at least 12 months between January 1, 2007, and December 31, 2008. Women with another cancer diagnosed before the breast cancer diagnosis and women without microscopically confirmed disease were excluded. Women who were diagnosed in Louisiana in 2005 were excluded from this analysis because of the disruption in SEER data collection following hurricane Katrina. We divided women into five groups characterized by the amount of time elapsed between their cancer diagnosis and the period of observation. We described their rates of use of tamoxifen and AIs from 2007 to 2008. See **Table 1** for a crosswalk between year of diagnosis and period of observation.

**Table 1:** Description of the cohorts and the number of older women with ductal carcinoma in situ and early invasive breast cancer in each cohort, 2007-2008\*

| Diagnosis Month              | Total  | Months since diagnosis        |                               |                               |                               |                               |
|------------------------------|--------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|
|                              |        | 0-12                          | 13-24                         | 25-36                         | 37-48                         | 49-60                         |
|                              |        | December 2006 - December 2007 | December 2005 - December 2006 | December 2004 - December 2005 | December 2003 - December 2004 | December 2002 - December 2003 |
| DCIS                         | 6,252  | 1,226                         | 1,337                         | 1,250                         | 1,242                         | 1,197                         |
| Early Invasive Breast Cancer | 27,378 | 5,556                         | 5,959                         | 5,365                         | 5,453                         | 5,045                         |

\* Limited to women enrolled in Part D in the SEER-Medicare data.

## Definitions

**DCIS:** We identified cases of DCIS using information on histology, stage, and behavior information collected by the SEER registries. Specifically, we included International Classification of Diseases for Oncology, Third Edition (ICD-O-3) histologies 8500, 8521, 8501, 8230, 8522, and 8523 with an ICD-O-3 behavior code of 2, and ICD-O-3 histology 8500 with an ICD-O-3 behavior code of 5.

**Early invasive breast cancer:** We defined early invasive breast cancer using SEER summary local stage and ICD-O-3 behavior code of 3. SEER stage takes into account all information available through the first course of treatment.

**Age:** We grouped women into five-year age groups by age at diagnosis.

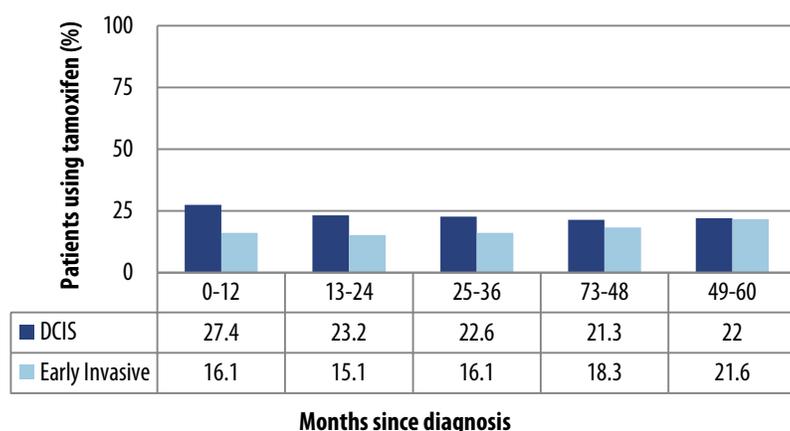
**Race/ethnicity:** We defined race using the SEER Race Recode Y variable. The SEER Origin variable was used to indicate Hispanic ethnicity among whites, resulting in the following race/ethnicity categories: white, white Hispanic, black, and Asian or Pacific Islander.

**Urban/rural:** We divided women into urban and rural groupings based on the county of residence using the 2003 Rural/Urban Continuum Codes from Economic Research Service (ERS), Department of Agriculture.<sup>9</sup> “Big Metro” refers to counties in metro areas with at least 1 million people. “Metro” refers to other counties in metro areas. “Urban” refers to counties not in metro areas with at least 20,000 people. “Less Urban” refers to counties with 2,500-19,999 people. Rural refers to counties with fewer than 2,500 people.<sup>9</sup>

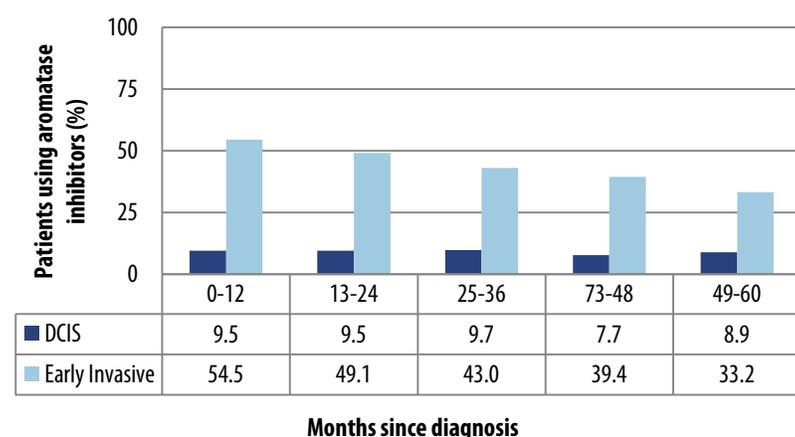
**Tumor size:** We defined tumor size using the extent of disease extension field for women diagnosed in 2002 and 2003, and the SEER collaborative staging tumor extension field for women diagnosed in 2004 or later.

**Figure 1:** Percentage of older women with ductal carcinoma in situ or early invasive breast cancer using endocrine therapy by months since diagnosis, 2007-2008

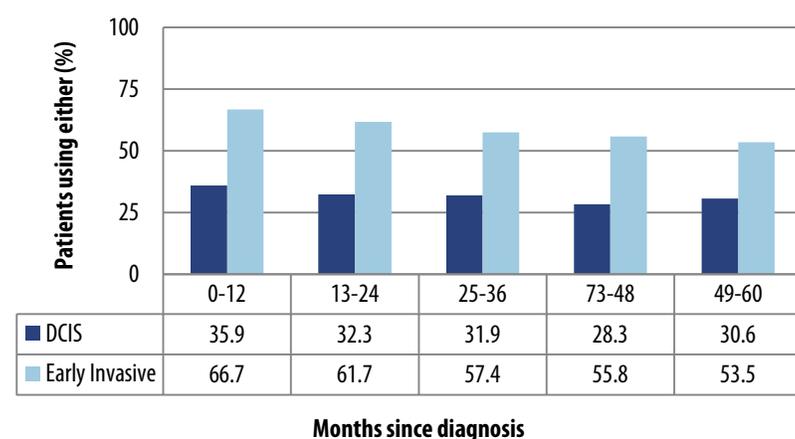
**1A. Tamoxifen Use**



**1B. Aromatase Inhibitor Use**



**1C. Either Tamoxifen or AI Use**



We report rates for microscopic, <1 cm, <2 cm, 2-5 cm, and >5 cm. Other categories are included in the cohort but not reported (e.g., unknown and diffuse).

**Grade:** We defined grade using the fields provided by SEER: well differentiated, moderately/intermediately differentiated, poorly differentiated, and undifferentiated/anaplastic. Unknowns are included but not reported.

**Receipt of surgery and RT:** The use of BCS or mastectomy was determined using the “Rx Summ-Surgery of the Primary Site” (sxprif1) variable (BCS: 20-24 and mastectomy: 40-80). We used the SEER Radiation variable to identify women receiving BCS who also received RT as part of their first course of treatment. We categorized treatments as: mastectomy, BCS+RT, and BCS alone. Women with a value of “Unknown” or “Recommended but unknown if received” are not included in this field.

**ER status:** SEER registries collect information about ER testing results. Women classified as ER status unknown may not have been tested.

**Part D enrollment:** We limited our cohort to women with Medicare Part D enrollment using values of “H,” “R,” “S,” or “E” on the monthly Plan Value Indicators (plan07\_01 – plan08\_12) to signal Part D enrollment. Only individuals enrolled in Part D during the entire 12 months of interest are included in our cohort. For example, to be included in the one to two years since diagnosis group, a woman must be enrolled in Part D during the entire 13-24 months following diagnosis, and this period must have occurred in its entirety between January 1, 2007, and December 31, 2008.

**Health maintenance organization**

**(HMO) enrollment:** We defined enrollment in an HMO based on the presence of an HMO Indicator (gho1-gho288) not equal to “0” or “4” for at least one month during the years since diagnosis category of interest.

**State assistance:** We considered recipients of State assistance to be those with a State Reported Dual Eligible Status Code monthly indicator (plan07\_01 – plan08\_12) between “01” and “09” for at least one month during the years since diagnosis category of interest.

**Endocrine therapy use:** Using the Part D data, we identified tamoxifen using Brand Name (bn) of TAMOXIFEN CITRATE or Generic Name (gnn) of TAMOXIFEN CITRATE. Likewise, we identified aromatase inhibitors using Brand Name of ARIMIDEX, AROMASIN, or FEMARA or Generic Name of ANASTROZOLE, EXEMESTANE, or LETROZOLE.

**RESULTS**

The 33,630 women in the SEER program who met our criteria for Part D enrollment were diagnosed with either DCIS or early invasive breast cancer between 2002 and 2007. Most of these women (81.4%) were diagnosed with early invasive breast cancer. The cohort we examine in this report consists of 6,252 women diagnosed with DCIS (approximately 1,200-1,300 in each month since diagnosis grouping) and 27,378 diagnosed with early invasive breast cancer (between 5,000 and 6,000 in each month since diagnosis grouping) (Table 1).

**Endocrine Therapy Use Patterns Among Patients With DCIS**

Among women with DCIS, the proportion using tamoxifen was higher than the proportion using AIs in all time periods. For example, in the first period, 27 percent of women were on tamoxifen, and 10 percent were on an AI. Tamoxifen use decreased slightly over time, while use of AIs was relatively stable (Figure 1).

Use varied by beneficiary demographic characteristics and followed similar patterns in each group. Use declined with age at diagnosis. Among women 49-60 months after diagnosis, 34.5 percent ages 65-69 at diagnosis were on either medication compared with 32.4 percent of women ages 70-74, 28.0 percent ages 75-79, and 16.3 percent ages 80-84 at diagnosis. Endocrine therapy use varied importantly by race. Among women 49-60 months after diagnosis, 40.2 percent of Hispanic white women were using therapy, as were 38.7 percent of black women, 26.8 percent of Asian/Pacific Islander women, and 27.3 percent of non-Hispanic white women (Table 2; Figure 2).

Rates varied by Medicare payer arrangement and receipt of State assistance. Rates of use were higher among women enrolled in fee-for-service (FFS) Medicare than among women enrolled in a Medicare HMO (38.7% vs. 32.1%) in the first year following diagnosis; however, other groups showed similar rates of use. In all groups, women who received State assistance used endocrine therapy at a higher rate than women without State assistance (Table 2).

Use of therapies varied by some but not all tumor characteristics. Use was highest among women with ER+ tumors (38.8 percent among women 49-60 months postdiagnosis), followed by women with tumors of unknown ER status and ER status not tested at the time of diagnosis (29.4 percent and 25.8 percent, respectively, among women 49-60 months postdiagnosis). Use was lowest among women with ER- tumors. Use did not vary greatly across tumor size or grade. In all groups, use was higher among women treated with BCS+RT than either mastectomy or BCS without RT (Table 2; Figure 3).

Endocrine therapy use did not vary consistently by population density; however, it did vary considerably by geography. For example, among women 49-60 months postdiagnosis, use was highest for women in Detroit (40%) and lowest for women in Seattle (22%; Table 2).

**Table 2:** Percentage of older women with ductal carcinoma in situ using endocrine therapy, by characteristic and months since diagnosis, 2007-2008<sup>†</sup>

|                           | 0-12 months | 13-24 months | 25-36 months | 37-48 months | 49-60 months |
|---------------------------|-------------|--------------|--------------|--------------|--------------|
| Overall                   | 35.9        | 32.3         | 31.9         | 28.3         | 30.6         |
| <b>Race</b>               |             |              |              |              |              |
| Non-Hispanic White        | 34.6        | 29.6         | 29.2         | 27.8         | 27.3         |
| Hispanic White            | 49.0        | 38.9         | 43.2         | 33.7         | 40.2         |
| Black                     | 35.1        | 39.0         | 37.4         | 32.4         | 38.7         |
| Asian/Pacific Islander    | 36.2        | 38.7         | 36.0         | 29.4         | 26.8         |
| <b>Age at Diagnosis</b>   |             |              |              |              |              |
| 65-69                     | 41.9        | 38.5         | 35.5         | 34.2         | 34.5         |
| 70-74                     | 42.4        | 36.9         | 35.6         | 30.4         | 32.4         |
| 75-79                     | 34.6        | 25.7         | 29.7         | 28.5         | 28.0         |
| 80-84                     | 21.8        | 20.4         | 20.1         | 17.9         | 16.3         |
| 85 +                      | 14.9        | 16.2         | 18.1         | 17.2         | *            |
| <b>State Aid</b>          |             |              |              |              |              |
| No                        | 34.6        | 30.0         | 29.8         | 27.6         | 28.4         |
| Yes                       | 41.3        | 41.0         | 38.5         | 35.1         | 33.2         |
| <b>HMO Enrollment</b>     |             |              |              |              |              |
| HMO                       | 32.1        | 31.5         | 30.3         | 27.0         | 29.2         |
| FFS                       | 38.7        | 32.1         | 32.1         | 30.3         | 29.4         |
| <b>Tumor Size</b>         |             |              |              |              |              |
| Microscopic               | 39.5        | *            | 41.3         | 26.1         | *            |
| <1 cm                     | 35.0        | 31.1         | 32.6         | 29.2         | 31.6         |
| <2 cm                     | 36.1        | 32.1         | 31.1         | 29.5         | 31.7         |
| 2-5 cm                    | 32.9        | 31.4         | 29.8         | 27.9         | 28.8         |
| >5 cm                     | 34.9        | 19.1         | 30.2         | 27.6         | 38.7         |
| <b>Tumor Grade</b>        |             |              |              |              |              |
| Well differentiated       | 36.0        | 34.3         | 36.8         | 30.2         | 28.2         |
| Moderately differentiated | 39.8        | 31.2         | 34.1         | 29.5         | 32.1         |
| Poorly differentiated     | 32.7        | 30.8         | 28.4         | 30.5         | 26.4         |
| Undifferentiated          | 27.7        | 28.9         | 26.5         | 27.2         | 27.5         |

|                           | 0-12 months | 13-24 months | 25-36 months | 37-48 months | 49-60 months |
|---------------------------|-------------|--------------|--------------|--------------|--------------|
| <b>ER Status</b>          |             |              |              |              |              |
| Not done                  | 33.5        | 27.2         | 35.8         | 26.1         | 25.8         |
| Positive                  | 43.9        | 40.1         | 35.7         | 34.2         | 38.8         |
| Negative                  | 11.8        | 8.3          | 13.0         | 13.8         | *            |
| Unknown                   | 28.8        | 27.2         | 23.8         | 33.0         | 29.4         |
| <b>Surgery</b>            |             |              |              |              |              |
| BCS alone                 | 29.9        | 26.7         | 30.4         | 24.2         | 22.4         |
| BCS + RT                  | 46.2        | 40.4         | 35.0         | 34.6         | 34.8         |
| Mastectomy                | 26.0        | 21.0         | 26.2         | 24.6         | 26.2         |
| <b>Registry</b>           |             |              |              |              |              |
| Atlanta                   | 42.9        | 45.2         | 40           | 34           | 32.6         |
| Connecticut               | 46.8        | 32.4         | 36.6         | 31.8         | 31.3         |
| Detroit                   | 42.3        | 47.8         | 33.8         | 39.2         | 40           |
| Greater California        | 31.9        | 25.8         | 32.9         | 27.8         | 22.9         |
| Hawaii                    | 33.3        | *            | *            | 35.1         | 36.7         |
| Iowa                      | 26.9        | 23.8         | 19.7         | 21.3         | 30.2         |
| Kentucky                  | 35.5        | 42.5         | 43.8         | 35.5         | 35.1         |
| Los Angeles               | 38          | 36.6         | 39.1         | 27.1         | 33.1         |
| Louisiana                 | 42.9        | 45.7         | †            | 35.1         | 25.4         |
| New Jersey                | 44.9        | 30.6         | 30.8         | 32.6         | 34.8         |
| New Mexico                | *           | *            | *            | *            | *            |
| San Francisco             | 25          | 26.5         | 25           | 19.5         | 23.9         |
| San Jose                  | 45.7        | 30.2         | 23.1         | 31           | 29.7         |
| Seattle                   | *           | *            | 13.8         | 23.5         | 22           |
| Utah                      | 34.3        | *            | *            | *            | *            |
| <b>Population Density</b> |             |              |              |              |              |
| Big metro                 | 35.3        | 32.0         | 31.7         | 29.5         | 29.7         |
| Metro                     | 37.7        | 30.6         | 29.9         | 28.3         | 27.9         |
| Nonmetro                  | 35.3        | 33.8         | 31.9         | 27.2         | 30.3         |

\* Numerator <11 or denominator <30.

† Louisiana cases diagnosed in 2005 are not reported due to Hurricane Katrina. Denominators can be found in Appendix A.

‡ Limited to women enrolled in Part D in the SEER-Medicare data.

BCS: Breast-conserving surgery.

HMO: Health maintenance organization (Medicare managed care).

FFS: Fee-for-service Medicare.

ER: Estrogen receptor.

## Endocrine Therapy Use Patterns Among Patients With Early Invasive Disease

Among women with early invasive breast cancer, the proportion of women using tamoxifen was lower than the proportion of women using AIs in all groups. For example, in the first 12 months after diagnosis, 16 percent of women were on tamoxifen and 55 percent were on an AI. Use of tamoxifen increased slightly as time from diagnosis increased, while use of AIs declined. Use of either type of endocrine therapy declined from 67 percent in women 0-12 months following diagnosis to 54 percent among women 49-60 months postdiagnosis (**Figure 1**).

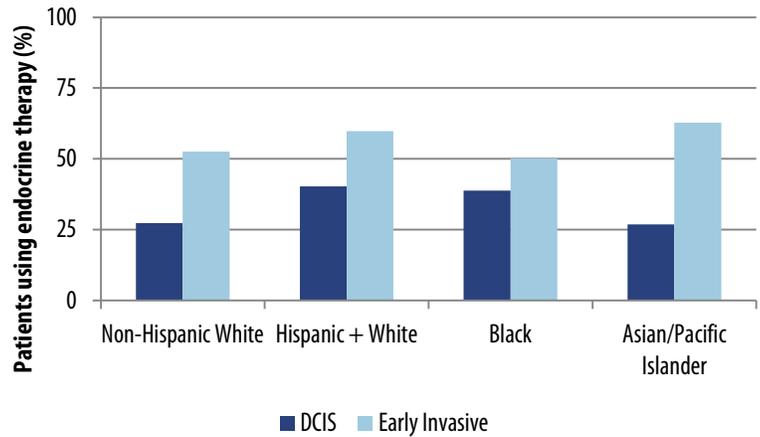
In all groups, use was associated with demographic characteristics. Use declined consistently with age at diagnosis. Use was highest among Hispanic Whites and Asian/Pacific Islander women, and lowest among black women. Non-Hispanic white women had the second lowest rate of use in all groups (**Table 3**).

Use of endocrine therapy also varied by tumor characteristics (**Figure 3**). Use was highest for women with ER+ tumors (60.5 percent among women 49-60 months postdiagnosis) and lowest for women with ER- tumors (11.5% in the same group). Women whose ER status was not tested or unknown were intermediate (35.8% and 54.2%, respectively, in the same group).

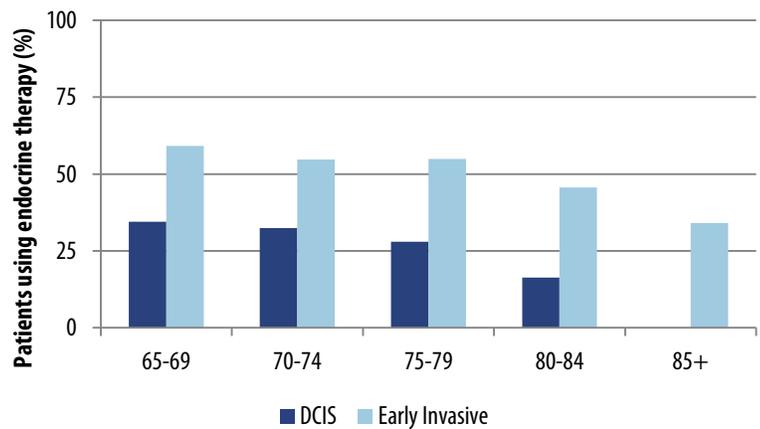
Endocrine therapy use was higher among women with well or moderately differentiated tumors (54.7% and 57.8%, respectively, among women 49-60 months postdiagnosis), and lowest for women with undifferentiated tumors (34.4% in the same group). Use increased with increasing tumor size (**Table 3**).

**Figure 2:** Percentage of older women with ductal carcinoma in situ or early invasive breast cancer using endocrine therapy in the fifth year following diagnosis, by demographic characteristics, 2007-2008

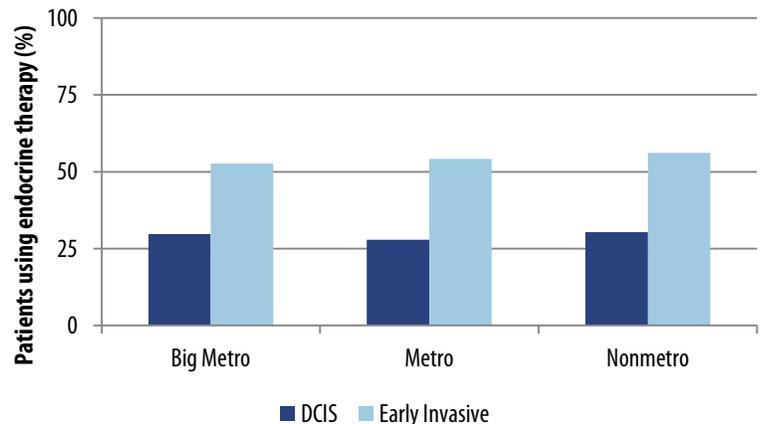
### 2A. Race/Ethnicity



### 2B. Age (Years)



### 2C. Population Density



**Table 3:** Percentage of older women with early invasive breast cancer using endocrine therapy, by characteristic and months since diagnosis, 2007-2008<sup>†</sup>

|                           | 0-12 months | 13-24 months | 25-36 months | 37-48 months | 49-60 months |
|---------------------------|-------------|--------------|--------------|--------------|--------------|
| Overall                   | 66.7        | 61.7         | 57.4         | 55.8         | 53.5         |
| <b>Race</b>               |             |              |              |              |              |
| Non-Hispanic White        | 66.4        | 61.0         | 56.7         | 54.4         | 52.5         |
| Hispanic White            | 70.6        | 68.9         | 64.2         | 69.0         | 59.8         |
| Black                     | 63.3        | 62.5         | 49.8         | 50.0         | 50.2         |
| Asian/Pacific Islander    | 68.7        | 63.7         | 60.2         | 64.4         | 62.7         |
| <b>Age at Diagnosis</b>   |             |              |              |              |              |
| 65-69                     | 72.5        | 67.4         | 63.0         | 61.4         | 59.2         |
| 70-74                     | 71.9        | 65.8         | 60.5         | 59.2         | 54.7         |
| 75-79                     | 67.3        | 61.7         | 57.9         | 54.2         | 54.9         |
| 80-84                     | 61.9        | 54.8         | 49.3         | 49.9         | 45.6         |
| 85 +                      | 45.9        | 46.2         | 43.3         | 39.9         | 34.1         |
| <b>State Aid</b>          |             |              |              |              |              |
| No                        | 67.1        | 61.4         | 57.0         | 55.5         | 54.2         |
| Yes                       | 64.9        | 63.0         | 58.9         | 57.1         | 50.5         |
| <b>HMO Enrollment</b>     |             |              |              |              |              |
| HMO                       | 68.8        | 62.1         | 57.8         | 55.5         | 53.3         |
| FFS                       | 65.1        | 61.5         | 57.0         | 56.0         | 53.6         |
| <b>Tumor Size</b>         |             |              |              |              |              |
| Microscopic               | 50.6        | 39.5         | 32.9         | 50.0         | 34.6         |
| <1 cm                     | 63.7        | 57.6         | 51.5         | 50.2         | 47.6         |
| <2 cm                     | 71.1        | 65.9         | 61.8         | 58.8         | 56.8         |
| 2-5 cm                    | 64.5        | 61.1         | 58.5         | 57.4         | 57.0         |
| >5 cm                     | 64.5        | 65.9         | 55.0         | 55.8         | 57.9         |
| <b>Tumor Grade</b>        |             |              |              |              |              |
| Well differentiated       | 71.0        | 65.0         | 61.1         | 57.5         | 54.7         |
| Moderately differentiated | 72.6        | 67.0         | 62.1         | 60.3         | 57.8         |
| Poorly differentiated     | 49.2        | 47.4         | 44.6         | 45.6         | 44.3         |
| Undifferentiated          | 41.7        | 43.1         | 44.0         | 38.5         | 34.4         |

|                           | 0-12 months | 13-24 months | 25-36 months | 37-48 months | 49-60 months |
|---------------------------|-------------|--------------|--------------|--------------|--------------|
| <b>ER Status</b>          |             |              |              |              |              |
| Not done                  | 53.0        | 37.2         | 49.5         | 45.9         | 35.8         |
| Positive                  | 76.5        | 70.8         | 66.0         | 63.8         | 60.5         |
| Negative                  | 9.6         | 8.8          | 8.8          | 8.8          | 11.5         |
| Unknown                   | 60.3        | 58.4         | 50.2         | 55.0         | 54.2         |
| <b>Surgery</b>            |             |              |              |              |              |
| BCS alone                 | 59.8        | 52.5         | 49.9         | 51.0         | 45.2         |
| BCS + RT                  | 72.8        | 66.2         | 61.4         | 58.2         | 55.2         |
| Mastectomy                | 62.7        | 61.6         | 56.2         | 55.1         | 55.7         |
| <b>Registry</b>           |             |              |              |              |              |
| Atlanta                   | 70.4        | 63.6         | 50           | 59.5         | 43.4         |
| Connecticut               | 65.9        | 65           | 61.5         | 59.8         | 61.2         |
| Detroit                   | 66.2        | 55.3         | 52.3         | 51.8         | 56.3         |
| Greater California        | 66.4        | 62.4         | 57           | 55.7         | 50.3         |
| Hawaii                    | 68          | 60.9         | 67.2         | 64.3         | 66.4         |
| Iowa                      | 58.7        | 51.2         | 44.1         | 44.8         | 54.2         |
| Kentucky                  | 65          | 64           | 65.5         | 57.2         | 60.8         |
| Los Angeles               | 70.7        | 64.3         | 59.5         | 61.7         | 58.5         |
| Louisiana                 | 70.5        | 65.9         | †            | 59.9         | 58.2         |
| New Jersey                | 71.0        | 63.9         | 62.1         | 59.4         | 54.8         |
| New Mexico                | 61.5        | 59           | 54.6         | 53.1         | 57.7         |
| San Francisco             | 65.7        | 65.4         | 59.7         | 53.9         | 47.3         |
| San Jose                  | 64.6        | 62.2         | 57.6         | 55.9         | 49.4         |
| Seattle                   | 63.5        | 53.7         | 45.6         | 41.7         | 43.6         |
| Utah                      | 59.7        | 56           | 56.4         | 48.7         | 48.9         |
| <b>Population Density</b> |             |              |              |              |              |
| Big metro                 | 68.2        | 63.2         | 57.5         | 56.6         | 52.7         |
| Metro                     | 64.3        | 59.9         | 57.6         | 55.0         | 54.2         |
| Non-metro                 | 63.8        | 57.5         | 56.3         | 53.5         | 56.2         |

<sup>†</sup> Louisiana cases diagnosed in 2005 are not reported due to Hurricane Katrina. Denominators can be found in Appendix B.

<sup>‡</sup> Limited to women enrolled in Part D in the SEER-Medicare data.

BCS: Breast-conserving surgery.

HMO: Health maintenance organization (Medicare managed care).

FFS: Fee-for-service Medicare.

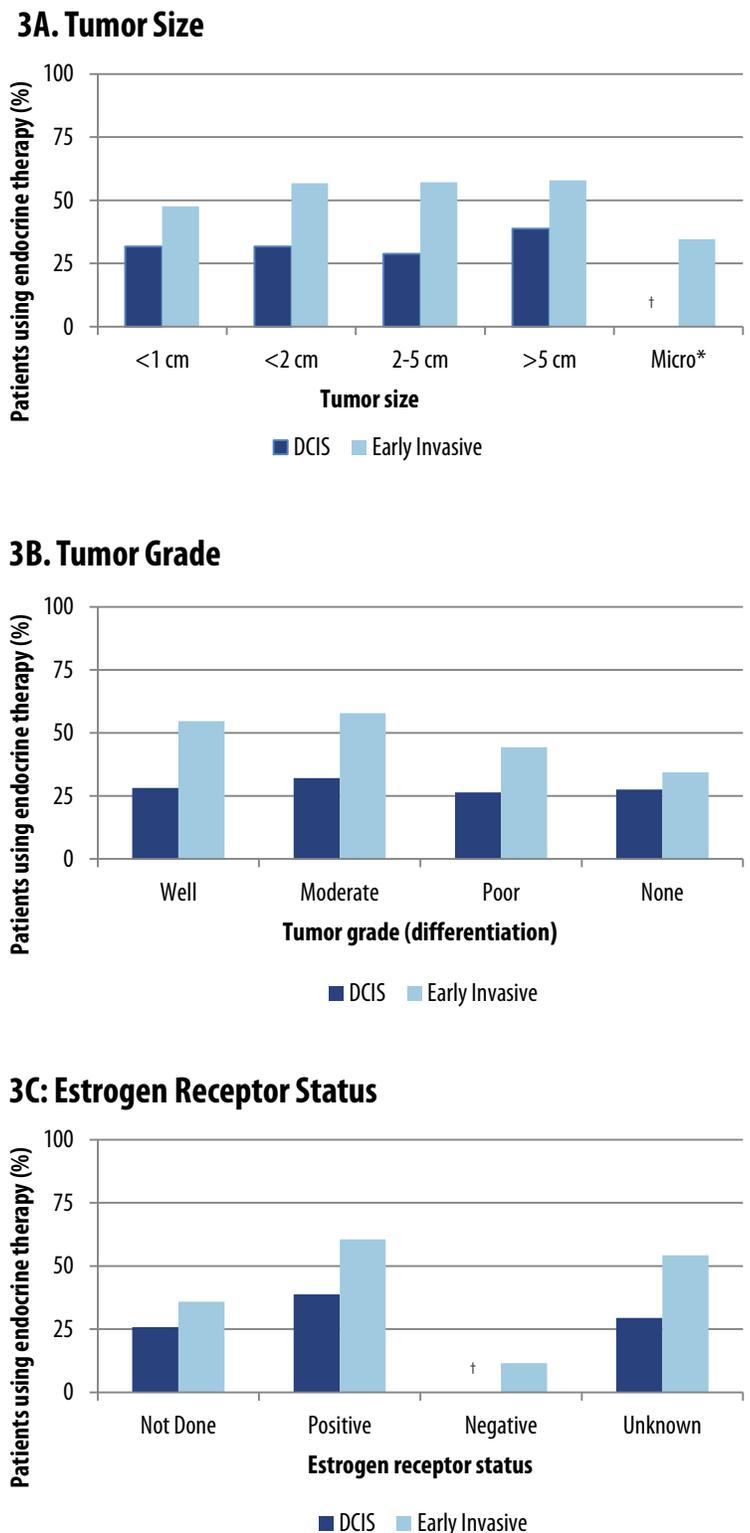
ER: Estrogen receptor.

Women treated with BCS+RT had higher rates of therapy use than women treated with mastectomy, though these rates converged by five years postdiagnosis. In all groups, women treated with BCS alone had the lowest rates of endocrine therapy use (Table 3).

While use of endocrine therapy varied considerably by geographic location, we found no consistent pattern of use associated with population density. Among women in the first year after diagnosis, Iowa had the lowest rate, at 58.7 percent, and New Jersey the highest, at 71.0 percent. Among women 49-60 months postdiagnosis, Atlanta had the lowest rate (43.4%) and Hawaii the highest (66.4%; Table 3).

Rates also varied by payer arrangement and receipt of State assistance. Unlike the DCIS population, rates of use are higher among women enrolled in Medicare HMO versus FFS (68.8% versus 65.1% among women in the first year after diagnosis). Again, unlike the DCIS population, women who received State assistance used endocrine therapy at a lower rate than women who did not (64.9% versus 67.1% among women in the first year after diagnosis; Table 3).

**Figure 3:** Percentage of women diagnosed with ductal carcinoma in situ or early invasive breast cancer using endocrine therapy in the fifth year following diagnosis, by tumor characteristics, 2007-2008



\*Micro: microscopic tumors.

† Not shown due to small numbers.

## Comparison of DCIS and Early Invasive Breast Cancer

Use of endocrine therapy following breast cancer diagnosis varied considerably between DCIS and early invasive breast cancer. Women with DCIS were more likely to be treated with tamoxifen than an AI; with early invasive breast cancer, the reverse pattern was seen, with AI use more common.

Across groups with varying time since diagnosis, endocrine therapy use for women with DCIS remained relatively stable, between 35.9 percent and 30.6 percent (**Figure 1**). Although use was higher in all groups for women with early invasive disease, we also observed a greater decline in use as time since diagnosis increased among women with early invasive disease. Yet no one particular amount of time since diagnosis was associated with a larger drop than other periods.

For both DCIS and early invasive breast cancer, use is associated with similar demographic characteristics. That is, use declines with increasing age at diagnosis (**Figure 2B**). Use of endocrine therapy among women with early invasive breast cancer is lowest for black women and similarly low for white women. Among women with DCIS use is lowest for Asian/Pacific Islander women (**Figure 2A**). Likewise, we observed considerable geographic variation but found no important patterns across levels of population density for both DCIS and early invasive breast cancer (**Figure 2C**).

Tumor characteristics were more strongly related to therapy use for women with early invasive disease than DCIS. With early invasive disease, use increased with increasing tumor size and declined with higher grade (**Figure 3**). For DCIS, patterns across both factors were less clear. For both groups, use was highest among women with ER+ tumors but was similar for women whose tumors were reported by SEER as untested or whose ER status was unknown. Use was lowest among ER- women, but notably, we observed that approximately 10 percent of early invasive cases with ER- tumors were treated with endocrine therapy in all time periods. Several possible explanations exist for these patterns. For example, some literature suggests that certain ER- tumors actually respond to endocrine therapy,<sup>10</sup> or there may be false negative ER tests.

The association between treatment with surgery, radiation therapy, and endocrine therapy use was strongly associated with adequate early treatment defined as either BCS+RT or mastectomy. For early invasive breast cancer, women treated with BCS alone were least likely to receive endocrine therapy. In the first three years following diagnosis of DCIS, women treated with mastectomy were least likely to receive endocrine. In the fourth and fifth years following diagnosis, women with DCIS who were treated with BCS alone were least likely to receive endocrine therapy (**Figure 4**).

The association between initial therapy with surgery and radiation and endocrine therapy use deserves further attention to ensure appropriate and optimal use.

## LIMITATIONS

Our study had limitations. First, it represents a series of five diagnostic cohorts rather than a single panel of patients. That is, different women are included in each of the five time groups. Thus we see some year-to-year differences where use rises slightly in a later year than in an earlier year.

We could not track therapy use over a five-year period for newly diagnosed women, because event data from the Medicare drug benefit were first available in 2007, the last year of incident cases for the SEER/Medicare dataset. Therefore, we cannot differentiate between women who began using endocrine therapy and discontinued use and those who never started taking endocrine therapy. However, our findings are consistent with a recent review by Banning and colleagues. That summary of 13 studies reported that between 15 percent and 53 percent of postmenopausal breast cancer patients were adherent to tamoxifen treatment one to five years after diagnosis, while 31 percent to 73 percent were adherent to AIs after one year of treatment.<sup>8</sup>

The women we included in this analysis are limited to those with Medicare Part D coverage, who represent approximately 50 percent of the newly diagnosed cases of DCIS or early invasive breast cancer. In general, this population is more likely to have low incomes than women with other forms of pharmacy coverage not included in the Part D data. We are not certain how this limitation affects inference in this study.

Finally, we measured prescriptions that were filled. However, we cannot be sure that women who fill prescriptions actually take all the medication as directed. For women who do not have prescriptions filled, we cannot determine whether the use was recommended by their provider or whether they began use of the therapy and discontinued use or never began therapy. Despite these limitations, this study provides important information about the use of endocrine therapies for women with incident DCIS and early invasive breast cancer.

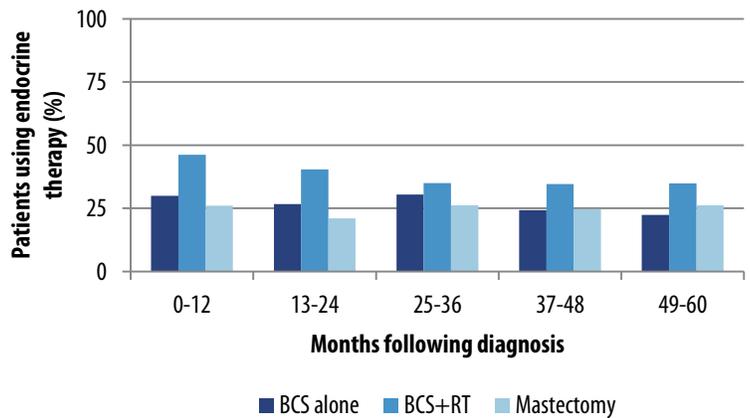
### CONCLUSION

Endocrine therapies have become an important strategy for preventing new primary breast cancers and invasive recurrences for women diagnosed with DCIS or early invasive breast cancer.<sup>3</sup> Our study found that the endocrine therapy of choice varied strongly by stage at diagnosis and that use of therapy varied by patient tumor and demographic characteristics. It appears that while rates of use are higher for women with early invasive cancers than for DCIS, the decline in use over the five years postdiagnosis is also greater.

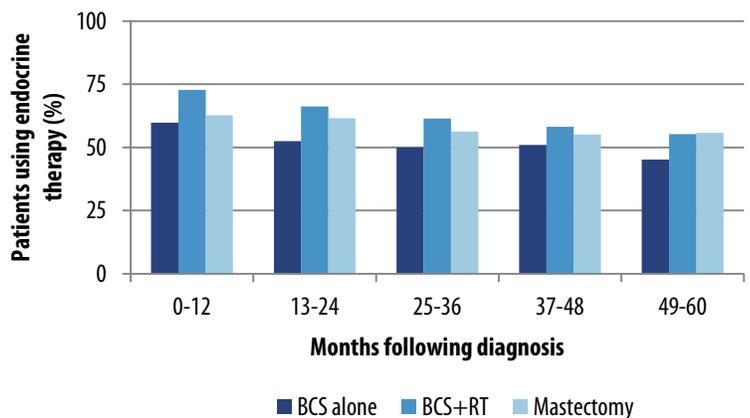
Further work is needed to understand the patient and provider factors associated with these patterns and to develop strategies promoting the most appropriate use of endocrine therapies for women diagnosed with breast cancer.

**Figure 4:** Percentage of women with ductal carcinoma in situ or early invasive breast cancer using endocrine therapy by surgery type and period of time after diagnosis, 2007-2008

#### 4A. Ductal carcinoma in situ



#### 4B. Early invasive breast cancer



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## AUTHORS

Beth A. Virnig, Ph.D., M.P.H.<sup>1</sup>  
 Michael T. Torchia, B.S.<sup>2</sup>  
 Stephanie L. Jarosek, R.N.<sup>1</sup>  
 Sara Durham, M.S.<sup>1</sup>  
 Todd M. Tuttle, M.D., M.S.<sup>2</sup>

<sup>1</sup> University of Minnesota School of Public Health, Division of Health Policy and Management, Minneapolis, MN.

<sup>2</sup> University of Minnesota School of Medicine, Department of Surgery, Minneapolis, MN.

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**Appendix A:** Number of older women with ductal carcinoma in situ using endocrine therapy, by characteristic and months since diagnosis, 2007-2008<sup>†</sup>

|                                 | 0-12 months | 13-24 months | 25-36 months | 37-48 months | 49-60 months |
|---------------------------------|-------------|--------------|--------------|--------------|--------------|
| <b>Overall</b>                  | 1,226       | 1,337        | 1,250        | 1,242        | 1,197        |
| <b>Race</b>                     |             |              |              |              |              |
| Non-Hispanic White              | 888         | 971          | 929          | 918          | 910          |
| Hispanic White                  | 102         | 95           | 111          | 95           | 82           |
| Black                           | 94          | 123          | 91           | 111          | 111          |
| Asian/Pacific Islander          | 116         | 106          | 89           | 102          | 82           |
| <b>Age at diagnosis (years)</b> |             |              |              |              |              |
| 65 - 69                         | 375         | 442          | 403          | 412          | 406          |
| 70 - 74                         | 321         | 371          | 340          | 326          | 318          |
| 75 - 79                         | 286         | 288          | 286          | 284          | 261          |
| 80 - 84                         | 170         | 162          | 149          | 156          | 153          |
| 85 +                            | 74          | 74           | 72           | 64           | 59           |
| <b>State Aid</b>                |             |              |              |              |              |
| No                              | 991         | 1108         | 1029         | 1020         | 968          |
| Yes                             | 235         | 229          | 221          | 222          | 229          |
| <b>HMO enrollment</b>           |             |              |              |              |              |
| HMO                             | 520         | 552          | 524          | 496          | 510          |
| FFS                             | 706         | 785          | 726          | 746          | 687          |
| <b>Size</b>                     |             |              |              |              |              |
| Microscopic                     | 38          | 40           | 46           | 46           | 48           |
| <1 cm                           | 363         | 408          | 353          | 363          | 297          |
| <2 cm                           | 288         | 305          | 267          | 264          | 249          |
| 2 - 5 cm                        | 173         | 191          | 215          | 179          | 160          |
| >5 cm                           | 43          | 47           | 43           | 58           | 31           |
| <b>Grade</b>                    |             |              |              |              |              |
| Well differentiated             | 125         | 137          | 133          | 139          | 110          |
| Moderately differentiated       | 435         | 477          | 402          | 393          | 368          |
| Poorly differentiated           | 336         | 373          | 331          | 315          | 295          |
| Undifferentiated                | 166         | 187          | 215          | 191          | 211          |

|                           | 0-12 months | 13-24 months | 25-36 months | 37-48 months | 49-60 months |
|---------------------------|-------------|--------------|--------------|--------------|--------------|
| <b>ER status</b>          |             |              |              |              |              |
| Not done                  | 176         | 228          | 318          | 395          | 454          |
| Positive                  | 743         | 786          | 631          | 509          | 276          |
| Negative                  | 195         | 204          | 177          | 145          | 55           |
| Unknown                   | 111         | 114          | 122          | 191          | 412          |
| <b>Surgery</b>            |             |              |              |              |              |
| BCS alone                 | 358         | 409          | 401          | 368          | 357          |
| BCS + RT                  | 543         | 589          | 529          | 547          | 520          |
| Mastectomy                | 308         | 314          | 298          | 305          | 298          |
| <b>Registry</b>           |             |              |              |              |              |
| Atlanta                   | 35          | 42           | 35           | 47           | 43           |
| Connecticut               | 77          | 71           | 93           | 66           | 64           |
| Detroit                   | 52          | 69           | 71           | 51           | 60           |
| Greater California        | 304         | 333          | 319          | 313          | 297          |
| Hawaii                    | 33          | 27           | 23           | 37           | 30           |
| Iowa                      | 67          | 80           | 61           | 80           | 63           |
| Kentucky                  | 62          | 73           | 73           | 62           | 57           |
| Los Angeles               | 158         | 153          | 169          | 140          | 139          |
| Louisiana                 | 63          | 70           | †            | 74           | 63           |
| New Jersey                | 136         | 160          | 143          | 132          | 138          |
| New Mexico                | *           | 20           | 23           | 22           | 20           |
| San Francisco             | 100         | 113          | 88           | 82           | 92           |
| San Jose                  | 46          | 43           | 52           | 42           | 37           |
| Seattle                   | 49          | 53           | 65           | 68           | 59           |
| Utah                      | 35          | 29           | 27           | 21           | 32           |
| <b>Population density</b> |             |              |              |              |              |
| Big metro                 | 780         | 878          | 860          | 799          | 788          |
| Metro                     | 310         | 320          | 274          | 307          | 287          |
| Nonmetro                  | 136         | 139          | 116          | 136          | 122          |

\* Numerator <11 or denominator <30.

† Louisiana cases diagnosed in 2005 are not reported due to Hurricane Katrina.

‡ Limited to women enrolled in Part D in the SEER-Medicare data.

BCS: Breast-conserving surgery.

HMO: Health maintenance organization (Medicare managed care).

FFS: Fee-for-service Medicare.

ER: Estrogen receptor.

**Appendix B:** Number of older women with early invasive disease using endocrine therapy, by characteristic and months since diagnosis, 2007-2008\*

|                                 | 0-12 months | 13-24 months | 25-36 months | 37-48 months | 49-60 months |
|---------------------------------|-------------|--------------|--------------|--------------|--------------|
| Overall                         | 5,566       | 5,959        | 5,365        | 5,453        | 5,045        |
| <b>Race</b>                     |             |              |              |              |              |
| Non-Hispanic White              | 4,307       | 4,631        | 4,216        | 4,368        | 4,063        |
| Hispanic White                  | 412         | 456          | 422          | 364          | 336          |
| Black                           | 368         | 371          | 287          | 340          | 281          |
| Asian/Pacific Islander          | 361         | 386          | 352          | 320          | 303          |
| <b>Age at diagnosis (years)</b> |             |              |              |              |              |
| 65 - 69                         | 1,542       | 1,643        | 1,500        | 1,539        | 1,440        |
| 70 - 74                         | 1,383       | 1,477        | 1,389        | 1,459        | 1,381        |
| 75 - 79                         | 1,164       | 1,326        | 1,164        | 1,226        | 1,210        |
| 80 - 84                         | 863         | 946          | 843          | 805          | 697          |
| 85 +                            | 614         | 567          | 469          | 424          | 317          |
| <b>State Aid</b>                |             |              |              |              |              |
| No                              | 4,514       | 4,803        | 4,353        | 4,374        | 4,067        |
| Yes                             | 1,052       | 1,156        | 1,012        | 1,079        | 978          |
| <b>HMO enrollment</b>           |             |              |              |              |              |
| HMO                             | 2,380       | 2,418        | 2,306        | 2,228        | 2,132        |
| FFS                             | 3,186       | 3,541        | 3,059        | 3,225        | 2,913        |
| <b>Size</b>                     |             |              |              |              |              |
| Microscopic                     | 87          | 76           | 73           | 74           | 104          |
| < 1cm                           | 1,481       | 1,677        | 1,494        | 1,557        | 1,359        |
| <2 cm                           | 2,374       | 2,470        | 2,267        | 2,293        | 2,163        |
| 2 - 5 cm                        | 1,390       | 1,493        | 1,330        | 1,319        | 1,115        |
| >5 cm                           | 138         | 129          | 100          | 95           | 107          |
| <b>Grade</b>                    |             |              |              |              |              |
| Well differentiated             | 1,665       | 1,709        | 1,546        | 1,606        | 1,488        |
| Moderately differentiated       | 2,441       | 2,612        | 2,326        | 2,320        | 2,084        |
| Poorly differentiated           | 1,120       | 1,212        | 1,119        | 1,065        | 964          |
| Undifferentiated                | 36          | 58           | 50           | 65           | 64           |

|                           | 0-12 months | 13-24 months | 25-36 months | 37-48 months | 49-60 months |
|---------------------------|-------------|--------------|--------------|--------------|--------------|
| <b>ER status</b>          |             |              |              |              |              |
| Not done                  | 83          | 113          | 99           | 159          | 120          |
| Positive                  | 4,516       | 4,827        | 4,293        | 4,270        | 3,722        |
| Negative                  | 726         | 752          | 705          | 684          | 582          |
| Unknown                   | 234         | 257          | 257          | 327          | 612          |
| <b>Surgery</b>            |             |              |              |              |              |
| BCS alone                 | 1,215       | 1,310        | 1,136        | 953          | 779          |
| BCS + RT                  | 2,527       | 2,777        | 2,622        | 2,667        | 2,516        |
| Mastectomy                | 1,730       | 1,767        | 1,528        | 1,739        | 1,655        |
| <b>Registry</b>           |             |              |              |              |              |
| Atlanta                   | 159         | 151          | 136          | 121          | 99           |
| Connecticut               | 273         | 349          | 278          | 333          | 268          |
| Detroit                   | 201         | 244          | 235          | 222          | 190          |
| Greater California        | 1,552       | 1,571        | 1,498        | 1,484        | 1,379        |
| Hawaii                    | 128         | 128          | 125          | 112          | 116          |
| Iowa                      | 346         | 346          | 322          | 355          | 323          |
| Kentucky                  | 311         | 314          | 316          | 271          | 232          |
| Los Angeles               | 663         | 717          | 729          | 643          | 614          |
| Louisiana                 | 295         | 296          | †            | 317          | 287          |
| New Jersey                | 566         | 651          | 612          | 599          | 529          |
| New Mexico                | 109         | 117          | 119          | 113          | 104          |
| San Francisco             | 370         | 433          | 365          | 345          | 366          |
| San Jose                  | 189         | 185          | 198          | 152          | 160          |
| Seattle                   | 277         | 311          | 287          | 266          | 273          |
| Utah                      | 119         | 134          | 110          | 115          | 94           |
| <b>Population density</b> |             |              |              |              |              |
| Big metro                 | 3,492       | 3,797        | 3,484        | 3,432        | 3,143        |
| Metro                     | 1,431       | 1,484        | 1,307        | 1,402        | 1,295        |
| Nonmetro                  | 641         | 678          | 574          | 619          | 607          |

\* Limited to women enrolled in Part D in the SEER-Medicare data.

† Louisiana cases diagnosed in 2005 are not reported due to Hurricane Katrina.

BCS: Breast-conserving surgery.

HMO: Health maintenance organization (Medicare managed care).

FFS: Fee-for-service Medicare.

ER: Estrogen receptor.