



YSC Responds to JAMA Article on Breast Cancer Incidence

An article published in the Journal of the American Medical Association (JAMA) on February 26, 2013, discusses the incidence of breast cancer in the United States and concludes that the number of young women presenting with metastatic disease at initial diagnosis has been increasing over time. Given the subject matter of this article, YSC believes it is important to share with our constituents what this article says and what it means for young women diagnosed with breast cancer. A more detailed [Summary of Article](#) is below.

In "[Incidence of Breast Cancer with Distant Involvement Among Women in the United States, 1976 to 2009](#)," [hereinafter "JAMA article"] the authors examined data from the U.S. National Cancer Institute Surveillance, Epidemiology, and End Results [\(SEER\) database](#) to find trends among breast cancer diagnoses. The authors observed a "small but statistically significant increase in incidence of breast cancer with distant involvement [metastasis to distant location such as bone, brain, lung, etc.] for women aged 25 to 39 years" of age. (JAMA article, at 805). This increase accounted for the women who presented with metastatic (Stage IV) disease at time of initial diagnosis. According to the SEER 9 database, the incidence of women in the U.S. aged 25 to 39 who presented with metastatic disease at initial diagnosis went from 1.53 per 100,000 women in 1976 to 2.9 per 100,000 women in 2009. The authors do not know the cause of these results and admit that further studies to corroborate their findings are necessary. For more details and explanation of this study, see [Explanation and Commentary](#).

So what does this study mean to YSC, to young women diagnosed with breast cancer, and to healthy young women? First, there is no cause for alarm or panic. As the authors of this article state, their observations need to be corroborated and if that can be done, then further research is needed to ascertain why these numbers appear to be rising. The JAMA article is a retrospective observational study, and as such, gives us very limited information. This study

61 Broadway, Suite 2235
New York, NY 10006

p 646.257.3000
877.YSC.1011

f 646.257.3030

youngsurvival.org

Young women facing breast cancer together.

does not and cannot explain why the distant diagnoses may be rising in young women. As the authors admit, those diagnosed with distant disease at the time of their initial diagnosis is “relatively small.” We also need to bear in mind the limitations of retrospective surveillance data. [SEER 9 data](#) only captures 10% of the U.S. population from nine specific areas that may or may not be representative of the whole country.

How does this study affect young women already diagnosed with breast cancer? It doesn't. This article does not address the risk of recurrence or metastasis for a young woman previously diagnosed with breast cancer. Its findings applied to metastatic disease at initial diagnosis and not recurrence or spread of disease.

How does this study affect healthy young women? The study does not warrant any change to YSC's position that all young women should be familiar with their breasts, know what is normal for their body, and go to their healthcare provider if they find something that is not typical. As the JAMA study revealed, the incidence of localized and regional disease in 25 to 39 year olds has not changed since the 1970s. From 2005-2009, the median age at diagnosis for cancer of the breast was 61 years of age. Approximately 0.0% were diagnosed under age 20; 1.8% between 20 and 34; and 9.9% between 35 and 44. See

<http://seer.cancer.gov/statfacts/html/breast.html#incidence-mortality>

Does this article show a need for breast cancer screening in women aged 25 to 39? No. Current screening methods are not effective in young women. Recent research calls into question the benefits of screening mammography for women under 50. Just last December, a paper by one of the JAMA article authors and Dr. Gilbert Welch showed the harms that mammography screening¹ has caused over the last three decades. See

<http://www.youngsurvival.org/blog/?p=2046>.

Last, but certainly not least, this study shows the need for young women to be informed about science, statistics and critical review of study reports and media summaries of those reports. If you are interested in learning more, we encourage you to consider attending Project LEAD, a training course offered by the National Breast Cancer Coalition, which is now accepting

¹ Screening refers to the routine testing of healthy women to check for the presence of disease. This is different from diagnostic mammograms, which are performed when women show signs (such as a lump) of breast cancer.

applications for its annual Institute. <http://www.breastcancerdeadline2020.org/get-involved/training/project-lead/>

Regardless of the exact number of young women diagnosed with metastatic disease at initial diagnosis, it is too many. There is an urgent need to study metastatic disease, especially in young women who are generally understudied and excluded from metastatic clinical trials. YSC has always emphasized the importance of researching breast cancer in young women and this article supports that need.

Summary of Article

In “Incidence of Breast Cancer with Distant Involvement Among Women in the United States, 1976 to 2009,” [hereinafter “JAMA article”] the authors examined data from the U.S. National Cancer Institute Surveillance, Epidemiology, and End Results (SEER) database to find trends among breast cancer diagnoses.² The authors observed a “small but statistically significant increase in incidence of breast cancer with distant involvement [metastasis to distant location such as bone, brain, lung, etc.] for women aged 25 to 39 years” of age. (JAMA article, 805). This increase accounted for the women who presented with metastatic (Stage IV) disease at time of initial diagnosis. According to the SEER 9 database, the incidence of women in the U.S. aged 25 to 39 who presented with metastatic disease at initial diagnosis went from 1.53 per 100,000 women in 1976 to 2.9 per 100,000 women in 2009.³

The authors observed that the increase of Stage IV breast cancer in women ages 25 to 39 was most pronounced in African American and non-Hispanic white women.⁴ (JAMA article, Figure 3) The incidence was higher in young women with estrogen receptor-positive breast cancer. (JAMA article, at 803-04) The authors also observed a slight rise in metastasis at initial

² Please see discussion below for details on the SEER database.

³ SEER data collection began in 1973. The authors chose to begin their analysis of SEER data at the year 1976, “to avoid the sharp uptick in early breast cancer detection that followed First Lady Betty Ford’s highly publicized breast cancer diagnosis in 1974.” (JAMA article, at 801) According to an email exchange with Kathleen Cronin, PhD, MPH of the National Cancer Institute, incidence of distant disease in women aged 25 to 39 was 1.7 out of 100,000 in 1975, higher than the incidence in 1976 (1.53 out of 100,000).

⁴ SEER did not start collecting racial/ethnicity data until 1992, in its SEER13 database.

diagnosis between ages 40-54 from 1976 to 2009. The rate of diagnosis of metastatic disease, as well as regional and local diagnoses, remained steady in all other age groups. Further, the rate of diagnosis of local and regional disease in women under 40 remained unchanged over time. (JAMA article, Figure 1) According to SEER18 data collected since 2000, the mean five year survival rate for women ages 25 to 39 with distant disease was 31.4% and 86.8% for localized and regional disease – a difference of 55%.

The authors do not know the cause of these results and admit that further studies to corroborate their findings are necessary. They offered a variety of possible explanations for their findings including: changes in the way we classify the stages of breast cancer; improvements in our diagnostic technology; or the use of more imaging at the initial doctor visits to look for spread of disease. The authors conclude their article by stating, “[t]he trajectory of the incidence trend predicts that an increasing number of young women in the United States will present with metastatic breast cancer in an age group that already has the worst prognosis, no recommended routine screening practice, the least health insurance, and the most potential years of life. Our finding requires corroboration and, if confirmed, study of potential causes.”

Explanation and Commentary

The SEER Program of the National Cancer Institute works to provide information on cancer statistics in an effort to reduce the burden of cancer among the U.S. Population. See <http://seer.cancer.gov/statistics/> Beginning in 1973, SEER collected data on cancer cases from various locations and sources throughout the United States. The authors of the recent JAMA article used primarily SEER 9 data, which is data recorded since 1973 at 9 locations in the United States that captured tumor registry information. These 9 registry databases were located in: Atlanta, GA; Connecticut; Detroit, MI; Hawaii; Iowa; New Mexico; San Francisco Oakland, CA; Seattle-Puget Sound, WA; and Utah. The SEER 9 database covers only about 10% of the U.S. population.⁵

⁵ The authors also used data from SEER 13 and SEER 18. SEER expanded their data collection in 1992, adding four more registries (SEER 13) and again in 2012, adding five more (SEER 18). These registries cover 15% and 28% of the U.S. population, respectively.

While surveillance data such as SEER can be useful for population overviews and estimates, it is difficult to use it to make conclusive statements. SEER 9 data, counting only 10% of the U.S. population, can only give us a suggestion about what the real numbers are in the rest of the country. Obviously populations are different in different parts of the U.S. and what we may be experiencing in Connecticut may not reflect what is happening in Iowa. Surveillance data also does not explain “why,” or causation. As another research article using SEER data stated, “Limitations of analyses of registry data such as ours include the lack of information on individual-level risk factor and/or screening information, standardized review of histopathologic subtypes and/or hormone receptor testing, and incomplete data collection. The study is descriptive, and we can only speculate about why trends have varied for demographic and tumor characteristics according to age-at-onset.” Qualitative Age Interactions (or Effect Modification) Suggest Different Pathways for Early-Onset and Late-onset Breast Cancers, Cancer Causes Control 18: 1197 (2007).

Indeed, the authors of the JAMA article do not have an explanation for this increase in metastatic incidence. With the advent and continual improvement of diagnosis methods and computers, our data collection abilities and processing of information may have simply gotten better and the reporting of data easier. More likely, we are better at finding metastatic disease at time of initial diagnosis. Currently when young women present with a lump, they are sent for baseline bone scans and screening chest x-rays to find out if metastatic disease is a factor. That was not typical practice in the 1970’s when SEER data collection began.

Even if the numbers reported in the JAMA article are accurate and representative of the entire U.S. population, it is still a small number of women ages 25 to 39 who present with metastatic disease at time of initial diagnosis. The authors admit that the absolute increase in incidence over the 34 years of SEER data is “relatively small.” Further, the JAMA article does not present the actual number of young women diagnosed with distant breast cancer between 1976 and 2009. Instead, they use SEER data to approximate the number of women diagnosed per 100,000. From conversations with the study authors, we know that they estimated these actual numbers by extrapolating the SEER results (1.53 and 2.9 per 100,000) to the entire U.S. population. Doing so, they estimated that approximately 300 young women were diagnosed with metastatic disease at time of initial diagnosis in 1976 and that rose to approximately 800 women

by 2009. Again, these are small numbers and these are estimates -- assuming that the other 90% of the United States population has had the same rates of breast cancer as the 10% recorded in the SEER 9 database locations. Kathleen Cronin, Branch Chief, Data Analysis and Interpretation Branch, Division of Cancer Control and Population Sciences at the NCI wrote to us: "In 1973, 30 (1.7 /100,000) women age 25-39 were diagnosed with distant stage breast cancer [and] in 2009 that number was 84 (2.9/100,000). So the numbers are small. However it does seem to be increasing."

We also advise caution when examining JAMA Article Figure 1. The graph on distant disease, which is at the far right of Figure 1, makes it look as though the amount of distant disease for women ages 25 to 39 is huge - larger than the amount of localized and regional disease for young women in the charts to the left. This is because this graph is shown in log scale. You have to look closely to see that while the Y axis of the first two graphs (localized and regional disease) start at 10 and go to 400, the Y axis on the distant disease graph starts at 1 and goes to 40. So these three graphs are not drawn to the same scale and the distant disease graph looks far worse than it is at first glance.

While it is true that we may be seeing a more accurate picture of distant disease at first presentation, we are also seeing an improvement in survival rates and we know that targeted therapies have helped us to improve 5 year survival. As The JAMA article and YSC's recent Research Think Tank clearly indicate, more research is needed on young women and breast cancer, with a particular need to focus on the population of young women living with metastatic disease. YSC will continue to advocate for and support research that significantly impacts the quality and quantity of life for all young women affected by breast cancer.