

# Differences in Risk of Subsequent Primary Cancers Between In Situ and Invasive Breast Cancer

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## Abstract

**Background:** Excess risk of subsequent cancers has been found among breast cancer patients. Previous population-based studies focused primarily on invasive cancer. The purpose of this study is to evaluate the difference in the risk of subsequent cancers between in situ and invasive breast cancer patients by race and age at diagnosis.

**Methods:** We included first primary female breast cancers diagnosed in 1992-2012 from SEER13. O/E and excess absolute risk (EAR) were calculated to assess the risk subsequent breast and all other cancers.

**Results:** Overall, the risk of subsequent breast cancers was higher for in situ (O/E = 2.50, EAR=50.5) than invasive breast cancers (O/E = 1.58, EAR=20.0). However a reversed pattern was noted for the risk of other subsequent cancers with in situ disease than invasive breast cancer.

The risk of subsequent breast cancer among in situ women increased over time, while the risk of subsequent other cancers decreased over time. Invasive breast cancer survivors had the lowest risk of developing any subsequent cancers 1-4 years post-diagnosis.

The risk of subsequent breast cancer decreased with advancing age; and black women had higher risks of subsequent breast cancers than white women for both in situ and invasive cases.

**Conclusions:** Excess risk of subsequent cancers varies by type of breast cancer (in situ/invasive), times from the diagnosis of the first cancer, age, and type of subsequent cancer.

## Introduction

Female breast cancer is the most commonly diagnosed cancer and the second leading cause of cancer death in the US women. The excess risk of subsequent cancers has been found among breast cancer patients. Previous population-based studies focused primarily on invasive breast cancer.

## Objectives

The purpose of this study is to evaluate the difference in the risk of subsequent breast and other cancers between in situ and invasive breast cancer patients by race and age at diagnosis.

## Methods

We included first primary female breast cancers diagnosed in 1992-2012 from SEER13. Observed number of subsequent primary cancers /expected number of subsequent primary cancers (O/E) and excess absolute risk (EAR) were calculated to assess the risk of subsequent breast and other cancer.

## Results

A total of 24,719 subsequent breast cancer and 36,537 subsequent other cancers were observed among women who had survived 2 months or longer after the diagnosis of the primary breast cancer (443,061 invasive, 96,656 in situ) in 1992-2012.

Overall, the risk of subsequent breast cancers was higher for in situ (O/E = 2.50, EAR=50.5) than invasive breast cancers (O/E = 1.58, EAR=20.0). However a reversed pattern was noted for the risk of other subsequent cancers with in situ disease having a lower risk (O/E = 0.99, EAR=-0.44) than invasive breast cancer (O/E = 1.08, EAR=7).

**Table 1. Risk of Subsequent Primary Cancers after Diagnosed Female Breast Cancer, SEER 1992-2012**

Malignant	< 1 year		1 - < 5 year		5 - < 10 year		10 + year		Total	
	O/E	(EAR) <sup>2</sup>	O/E	(EAR) <sup>2</sup>	O/E	(EAR) <sup>2</sup>	O/E	(EAR) <sup>2</sup>	O/E	(EAR) <sup>2</sup>
All sites	1.27#	28.6	1.14#	15.8	1.24#	29.1	1.34#	46.4	1.23#	27.0
All excluding FB	1.17#	12.1	1.06#	4.9	1.08#	7.5	1.08#	8.1	1.08#	7.0
Female Breast	1.52#	16.5	1.33#	10.9	1.62#	21.7	2.03#	38.4	1.58#	20.0
Corpus and uterus	1.26#	1.7	1.35#	2.4	1.53#	3.9	1.48#	4.0	1.42#	3.1
Ovary	1.23#	0.8	1.20#	0.7	1.19#	0.7	1.22#	0.9	1.20#	0.8
Leukemia	1.04	0.1	1.74#	2.0	1.15#	0.5	1.07	0.2	1.34#	1.0
In Situ										
All sites	1.60#	56.9	1.48#	48.8	1.44#	51.0	1.36#	47.4	1.45#	50.0
All excluding FB	1.17#	11.0	1.02	1.5	0.97	-2.2	0.93#	-7.2	0.99	-0.4
Female Breast	2.52#	46.0	2.48#	47.3	2.54#	53.2	2.47#	54.6	2.50#	50.5
Corpus and uterus	1.24	1.5	1.28#	1.9	1.19#	1.4	1.29#	2.4	1.25#	1.8
Ovary	1.28	0.9	1.12	0.4	1.15	0.5	0.94	-0.3	1.1	0.4
Leukemia	0.63	-0.8	1.18	0.4	1.23	0.6	0.88	-0.4	1.08	0.2

O/E: observed number of subsequent primary cancers /expected number of subsequent primary cancer.

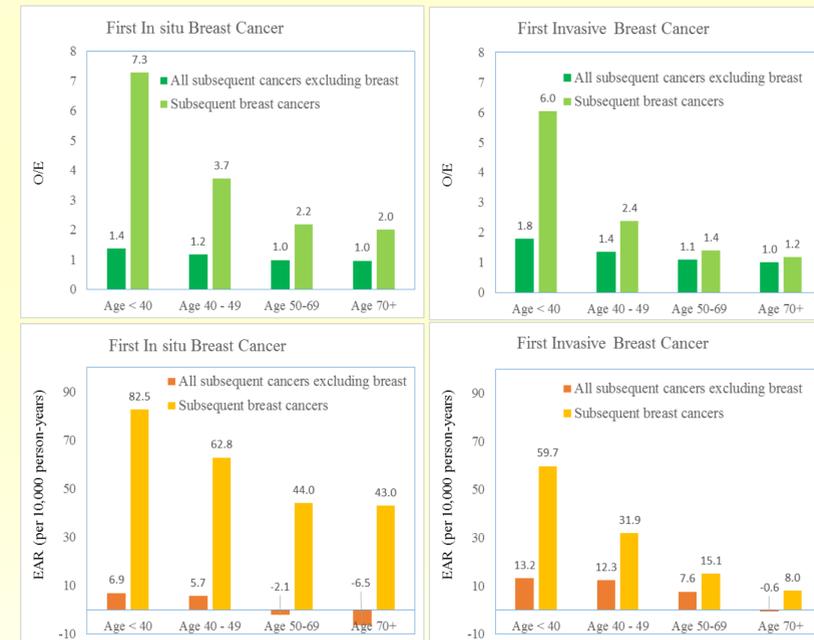
# P < 0.05, O/E is significantly different from 1.

Excess absolute risk (EAR) = (O-E)\*10,000/person-years at risk

The EAR of subsequent breast cancer among in situ patients increased over time (follow-up year <1, 1-4, 5-9, and 10+, EAR = 46, 47, 53, 55, respectively), while the risk of subsequent other cancers decreased over time (follow-up year <1, 1-4, 5-9, and 10+, EAR = 11, 2, -2, -7, respectively).

Invasive breast cancer survivors had the lowest risk of developing any subsequent cancers in 1-4 years post-diagnosis.

**Figure 1. O/E ratios and EAR of subsequent primary cancer after female breast cancers by Age, SEER 1992-2012.**



The risk of subsequent breast cancer decreased with advancing age for both in situ (age < 40 years, age 40-49, age 50-69, age 70+; EAR =82.5, 62.8, 44.0, 43.0; O/E =7.3, 3.7, 2.2, 2.0, respectively) and invasive breast cancers (age < 40 years, age 40-49, age 50-69, age 70+; EAR =59.7, 31.9, 15.1, 8.0; O/E =1.8, 1.4, 1.1, 1.0, respectively).

Black women had higher risks of subsequent breast cancers than white women for both in situ (O/E =3.5, EAR =78.2 versus O/E=2.4, EAR=47.1) and invasive breast cancers (O/E =2.5, EAR=44.9 versus O/E=1.5, EAR=17.2). API and others race group had highest risks of subsequent other cancers.

**Figure 2. O/E ratios and EAR of subsequent primary cancer after female breast cancers by Race, SEER 1992-2012.**



## Conclusions

1. Women with primary breast cancer (both in situ and invasive) had a substantially higher risk of developing subsequent breast cancers than any other cancers.
2. Women with in situ breast cancers had higher risk of subsequent breast cancer than that with invasive breast cancer, and lower risk of subsequent other cancers.
3. Women diagnosed with breast cancer at younger age had higher risk of subsequent breast than their counterparts diagnosed at older age. .
4. Black women had higher risks of subsequent breast cancer and all other types of cancer than white women.

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