

Breast cancer incidence rates in US women are no longer declining

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Running title: Breast cancer incidence rates in US women

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Abstract

Background: Several publications reported breast cancer incidence rates continued to decrease among white women, following the decline of about 7% from 2002-2003. However, none of these reports exclusively examined the trend after 2003. In this paper, we examined breast cancer incidence rates among non-Hispanic (NH) white women from 2003-2007 to determine whether the decrease in breast cancer incidence rates indeed persisted through 2007. In addition, we present breast cancer incidence trends for NH black and Hispanic women and postmenopausal hormone use for all three racial/ethnic groups.

Methods: Breast cancer incidence rates were calculated by race/ethnicity, age and ER status using data from the Surveillance, Epidemiology, and End Results (SEER) 12 registries for 2000-2007. Prevalence of postmenopausal hormone use was calculated using National Health Interview Survey data from 2000, 2005, and 2008.

Results: From 2003-2007, overall breast cancer incidence rates did not change significantly among NH white women in any age group. However, rates increased (2.7% per year) for ER+ breast cancers in ages 40-49, and decreased for ER- breast cancers in ages 40-49 and 60-69. Similarly, overall breast cancer incidence rates did not change significantly for black and Hispanic women. Hormone use continued to decrease from 2005 to 2008 in all groups, although the decreases were smaller compared to those from 2000 to 2005.

Conclusions: The sharp decline in breast cancer incidence rates that occurred from 2002-2003 among NH white women did not continue through 2007.

Impact: Further studies are needed to better understand the recent breast cancer trends.

Introduction

Breast cancer incidence rates among US white women remarkably decreased by about 7% between 2002 and 2003, with the decrease more pronounced for women ages 50-69 than for other age groups and for ER+ tumors than for ER- tumors (1-2). This decrease was temporally related to the dramatic drop in the use of postmenopausal hormone therapy (HT) following the publication of the Women's Health Initiative (WHI) study findings in July 2002 on the adverse health effects of combined HT use, including increased risk of breast cancer (3-4). Several recent publications reported female breast cancer incidence rates continued to decrease among white women (5-8). However, none of these studies exclusively examined the trend after 2003.

In this paper, we examined breast cancer incidence rates among non-Hispanic (NH) white women from 2003 through 2007 by age and hormone receptor status (ER+ or ER-) to determine whether the decrease in breast cancer incidence rates indeed persisted through 2007. In addition, we present data on recent breast cancer trends for NH black and Hispanic women by age and ER status, and data on postmenopausal HT-use by age for all three racial/ethnic groups for 2000, 2005, and 2008.

Methods

Data on female invasive breast cancer incidence were obtained from the National Cancer Institute's Surveillance, Epidemiology and End Results (SEER) 12 registries for the years 2000-2007 (9). Incidence rates were calculated for NH whites, NH blacks, and Hispanics. We excluded cases from the Alaska native registry following guidelines from SEER for producing statistics by Hispanic ethnicity. Incidence data for Hispanics are based on the North American Association of

Central Cancer Registries (NAACCR) Hispanic Identification Algorithm (NHIA). Incidence rates were also stratified by age at diagnosis (ages ≥ 30 , 30-39, 40-49, 50-59, 60-69, 70+) and estrogen receptor status (ER+ and ER-). All rates were adjusted for reporting delays using SEER 13-9 adjustment ratios. Delay adjustment ratios are not available for Hispanics, thus adjustment ratios for whites were used. The percentage of cases with missing ER status ranged from 18% in 2000 to 7% in 2007, therefore we imputed ER status for those with missing information using chained equation methods (10). The following covariates were used to impute ER status: age, SEER registry, year of diagnosis, race/ethnicity, progesterone receptor status, tumor size, histology, lymph node status, and 2000 county level poverty. To assess recent breast cancer trends following the sharp decrease between 2002-2003, we used Joinpoint Regression Program to fit a log-linear model to the age-standardized incidence rates from 2003 through 2007 (11). Breast cancer incidence rates were also plotted against year of diagnosis beginning in 2000 for visual inspection of the rates before and after the sharp decrease between 2002 and 2003 (noted by a dashed line in 2003 on the figures).

We also present data on HT use by hysterectomy status, race/ethnicity, and age (50+, 50-59, 60-69, and 70+) from the National Health Interview Survey for 2000, 2005, and 2008. The question on hormone therapy use changed from "Are you currently taking hormone replacement therapy?" in the 2000 and 2005 surveys to "Are you currently taking hormone replacement therapy for menopause?" in the 2008 survey. We used hysterectomy status as a surrogate for the type of hormone therapy used based on clinical practice guidelines that recommend estrogen and progestin (E+P) for women with a uterus and estrogen only (E only) therapy for women without a uterus (12).

Results

Figure 1 shows female breast cancer incidence rates by race/ethnicity from 2000-2007. The sharp decline between 2002 and 2003 in breast cancer incidence rates in NH white women has not continued through 2007. When a linear trend was fitted to the data from 2003-2007, there was no significant change ($p=0.46$) in the incidences rate for breast cancer among NH white women. NH Black and Hispanic women did not experience the steep drop in incidence from 2002-2003 and there were no significant changes in incidence rates from 2003-2007.

Incidence rates for NH white women by age at diagnosis for all breast cancers and for ER+ and ER- breast cancers separately are shown in Figure 2. Overall breast cancer incidence rates did not change significantly from 2003-2007 among NH white women in any age group (Table S1). However, the incidence rate in NH white women ages 60-69 increased from 402.9 per 100,000 in 2006 to 422.2 in 2007, an increase of 4.8%; it remains to be seen if this trend will continue. Trends for ER+ breast tumors are generally similar to trends for overall rates because they account for the majority of cases. However, among NH white women ages 40-49 rates of ER+ breast cancer significantly increased by an average of 2.7% per year, from 122.5 in 2003 to 135.3 in 2007. In contrast, ER- breast cancer rates decreased in every age group, although the trends were statistically significant only for ages 40-49 (5.7% per year) and 60-69 (2.3% per year) (Table S1).

Figure 3 compares breast cancer incidence rates by age of diagnosis and ER status for NH white, NH black, and Hispanic women. Overall breast cancer rates and ER+ breast cancer rates are highest among NH white women, followed by NH black and Hispanic women in every age group (except rates of overall breast cancer in ages 30-39 are comparable between whites

and blacks). Similar to white women, there were no significant changes in overall breast cancer incidence rates among NH black and Hispanic women in any age group during 2003-2007 (Table S1). However, incidence rates for ER+ breast cancers among NH black women ages 40-49 increased (5.2% per year) during 2003-2007. We also noted non-significant increases in ER+ breast cancer incidence rates from 2005 to 2007 among NH black women: from 129.9 to 160.5 for ages 50-59 and from 218.3 to 261.8 for ages 60-69.

In contrast to the pattern for ER+ breast cancer, NH black women have the highest rates of ER- breast cancer in every age group compared to NH white and Hispanic women. Though not statistically significant, ER- breast cancer rates during 2003-2007 appear to have increased in NH black women ages 60-69, whereas rates seem to have decreased among NH black women ages 30-39, 40-49, and 50-59.

Tables 1 and 2 present the prevalence of HT use by race/ethnicity and age among women without and with hysterectomy, respectively. Combined estrogen and progestin (E+P) use was highest among NH white women, followed by Hispanic, and NH black women (Table 1). E+P use continued to decline over this time interval, although the decreases from 2005 to 2008 were generally smaller in both absolute and relative terms, compared to the decreases from 2000 to 2005. By 2008, only 2.8% of NH white women ages 50 and older, 1.5% of Hispanic and 0.9% of NH black women used E+P therapy. Use of estrogen alone (E only) was more common than E+P and use was highest among NH white women, followed by NH Black and Hispanic women (Table 2). Similar declines in E only use were observed among each age and racial/ethnic group.

Discussion

Overall breast cancer incidence rates among NH white women did not continue to decrease after 2003. Our results are consistent with findings from a recent study from Canada and other non-population based studies in the US. Breast cancer incidence rates in Canadian women began to increase around 2004/2005, following a decline that began in 2002 (13). A US study based on data from the Kaiser Permanente Northwest healthcare system reported decreasing joinpoint trends from 2000-2006 (14). However, examination of the data year by year showed that the decrease was halted in 2004 in older women and rates may have increased among women ages 45-59 through 2006 (14). Another small study of NH white women from Marin County, California reported a non-significant increase in breast cancer incidence rates (particularly ER+ breast cancer) from 2004-2007 (15).

There are several possible explanations for the recent stabilization in breast cancer incidence rates among NH white women in the US. First, menopausal hormones are thought to promote the growth of hormone-sensitive tumors and withdrawal of HT therapy may delay diagnosis of occult breast tumors (1). However, the absolute decrease in HT use after 2003 may not have been large enough to continue delaying diagnoses. For example, among NH white women ages 50-59, E+P use decreased from 7.5% in 2005 to 4.2% in 2008, compared to an absolute decrease of 15% between 2000 and 2005 (Table 1). Second, the stable trends in incidence rates may reflect improved sensitivity of mammography without influence of HT, as HT increases breast density (16) and compromises the diagnostic performance of mammograms and breast biopsies (17). It may also in part reflect the relatively stable rates of screening mammography in the US since 2000 (18).

While incidence rates for ER+ tumors stabilized (overall) or increased (ages 40-49), rates for ER- breast cancer rates generally decreased during 2003-2007 among NH white women.

Previous studies have also documented declines in ER- breast cancer rates among SEER and other predominantly white populations (2, 7, 14, 19-21). These declines may reflect changes in the classification of hormone receptor status of breast tumors. Prior to the release of guidelines by ASCO/College of American Pathologists in 2010, there were no national or international guidelines for hormone receptor testing (22). With the inception of the new guidelines, the cutoff value for determining positivity has now been established as 1%, but cutoffs as high as 10% had previously been used.

Similar to white women, ER+ breast cancer rates significantly increased among NH black women ages 40-49. Non-significant increases in ER+ rates were also observed among NH black women ages 50-69. Consistent with previous studies (20, 23), we also found a non-significant increase in ER- breast cancer in black women, although in our study the increase was limited to women ages 60-69. It is not clear why ER+ and ER- breast cancer rates among black women may have increased for certain age groups. One hypothesis is that recent breast cancer incidence trends in black women reflect trends in the prevalence of obesity, which increased through the mid-2000s (20). Also, reasons for the higher rates of ER- breast cancer in black women compared to white and Hispanic women are not fully understood, but are thought to reflect a complex interaction of genetic, environmental, and behavioral factors (24).

This study has several strengths and limitations. This is a descriptive study of US population-based breast cancer incidence rates from the 12 SEER registries with high quality data, representing 14% of the US population. Another important strength of this study was our

imputation of ER status. Completeness of ER status continues to improve since SEER began collecting the variable in 1990; however, information is still missing from a significant proportion of cases, particularly among older women and racial/ethnic minorities. Our interpretation of recent breast cancer trends is limited because we cannot directly relate cases to screening or risk factor behaviors. In addition, information on the type of hormone therapy used was not directly available from the NHIS in 2000, 2005, and 2008. However, this information was explicitly asked in the survey in 1999 and prevalence estimates from 1999 (data not shown) and our estimates for 2000 were similar. Another limitation of this study was our statistical power to detect subtle trends in breast cancer incidence in age-specific analyses of NH black and Hispanic women due to smaller case counts, as well as for the less prevalent ER- breast cancers.

Conclusion

In summary, the sharp decline in breast cancer incidence rates that occurred from 2002 to 2003 among NH white women did not continue through 2007. Furthermore, no significant changes in overall breast cancer incidence rates occurred during 2003-2007 among NH white, NH black, and Hispanic women of any age group.

Figure Legend

Figure 1. Delay-adjusted breast cancer incidence rates by race/ethnicity, 2000-2007

Figure 2. Delay-adjusted breast cancer incidence rates* by age and estrogen (ER) receptor status, non-Hispanic white women, 2000-2007

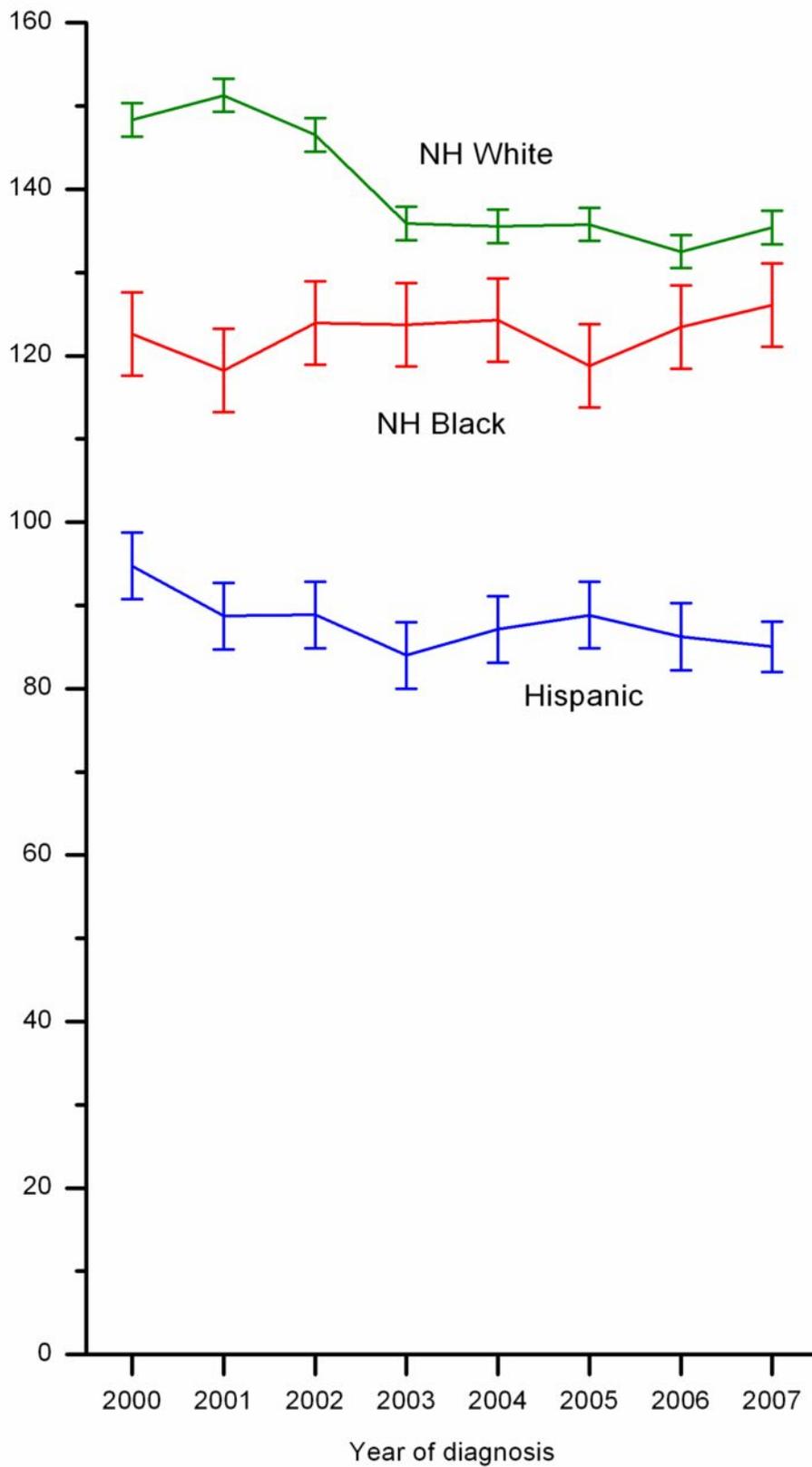
Figure 3. Delay-adjusted breast cancer incidence rates* by estrogen receptor (ER) status†, age, and race/ethnicity, 2000-2007

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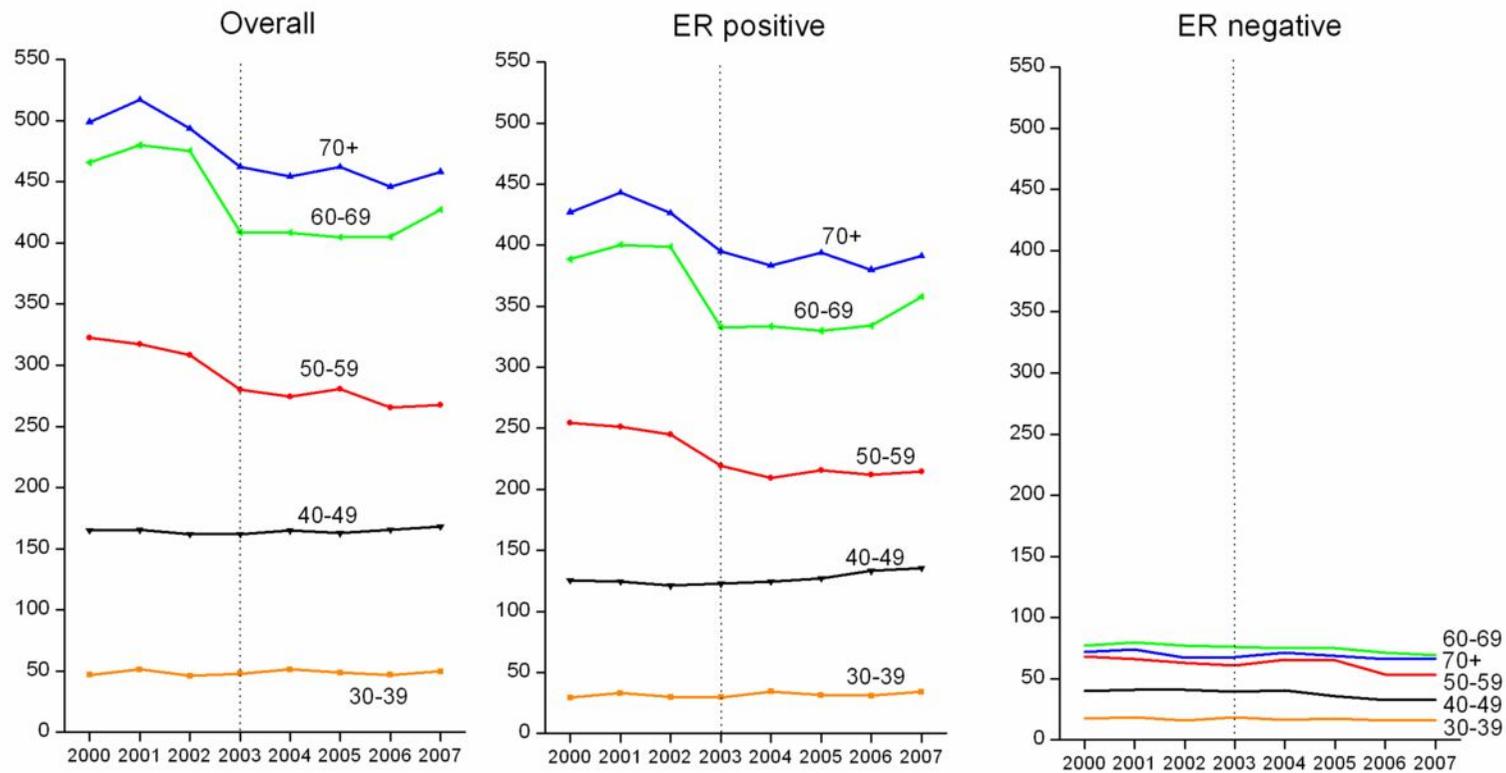
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Figure 1.



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

Figure 2.

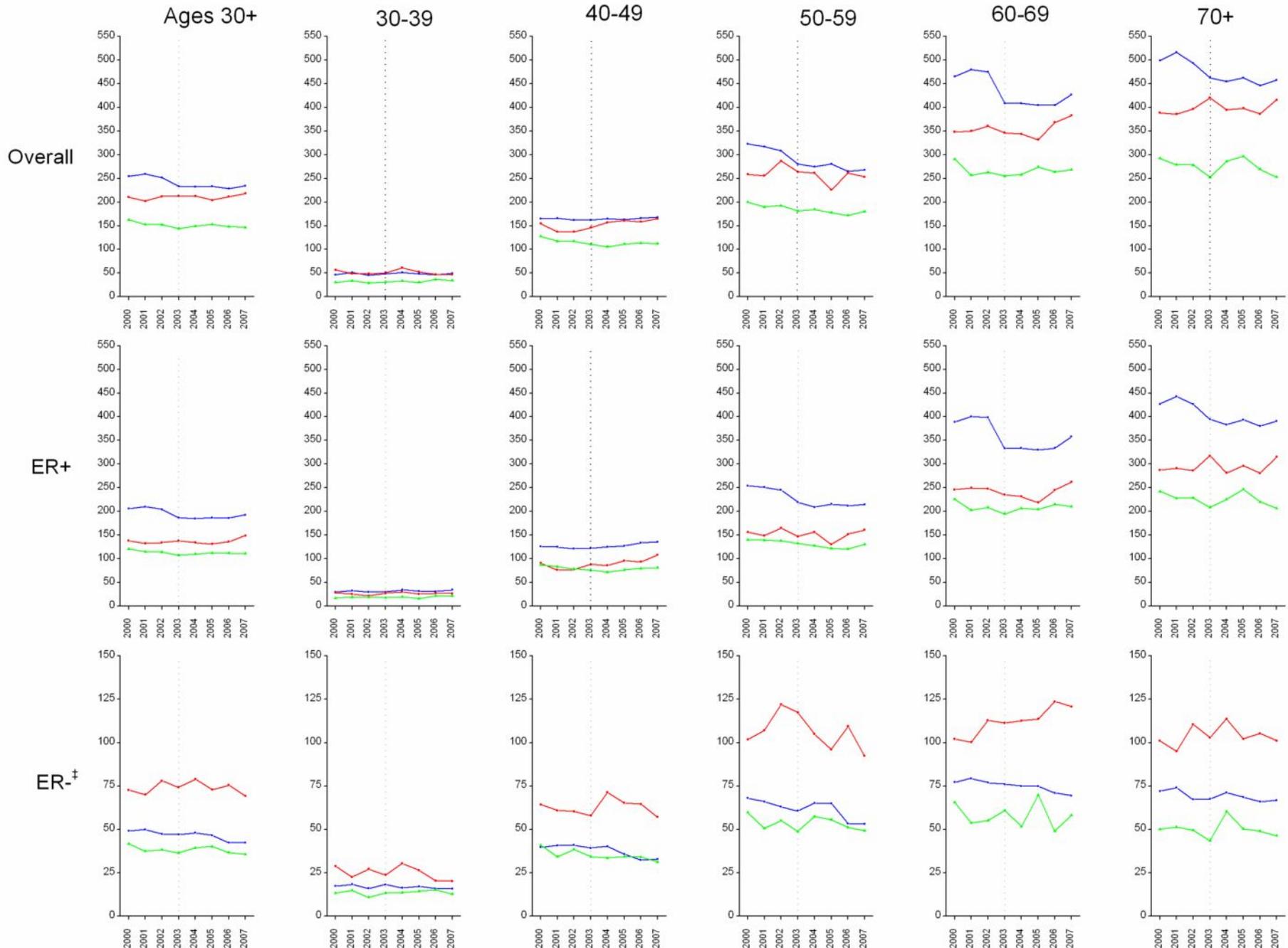


*Rates are per 100,000 and age adjusted to the 2000 US standard population.

†ER status was imputed for those with missing information.

Figure 3.

■ Non-Hispanic White ● Non-Hispanic Black ▲ Hispanic



*Rates and per 100,000 and age adjusted to the 2000 US standard population.

†ER status was imputed for those with missing information.

‡A tumor score was used to place ER- into ER-‡ and ER+ into ER+.

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Table 1. Trends in use of menopausal hormone therapy (estrogen + progestin) among US women without hysterectomy, by age and race/ethnicity, 2000-2008

	NH White		NH Black		Hispanic	
	%	95% CI	%	95% CI	%	95% CI
Ages 50+						
2000	13.8	(12.8 - 14.9)	4.2	(2.9 - 6.1)	10.4	(7.7 - 13.8)
2005	5.1	(4.5 - 5.8)	1.2	(0.7 - 2.1)	4.2	(2.9 - 6.1)
2008	2.8	(2.3 - 3.5)	0.9	(0.3 - 2.2)	1.5	(0.7 - 3.1)
Ages 50-59						
2000	22.5	(20.5 - 24.6)	7.0	(4.6 - 10.5)	18.1	(12.8 - 25.0)
2005	7.5	(6.3 - 8.8)	2.1	(1.1 - 4.0)	5.0	(3.1 - 8.0)
2008	4.2	(3.0 - 5.8)	1.2	(0.3 - 3.9)	1.4	(0.5 - 4.1)
Ages 60-69						
2000	12.9	(10.9 - 15.1)	3.2	(1.4 - 7.1)	7.4	(4.3 - 12.4)
2005	5.1	(4.0 - 6.6)	0.9	(0.3 - 2.4)	1.6	(0.5 - 5.1)
2008	3.0	(2.1 - 4.2)	1.1	(0.2 - 5.0)	2.6	(1.0 - 6.5)
Ages 70+						
2000	5.4	(4.4 - 6.6)	0.8	(0.2 - 2.5)	1.4	(0.4 - 4.5)
2005	2.1	(1.4 - 3.1)	0.0	--	5.5	(2.0 - 14.1)
2008	1.1	(0.6 - 2.0)	0.0	--	0.7	(0.1 - 5.1)

Source: National Health Interview Survey.

Note: Survey questions from 2000 and 2005 are not directly comparable to 2008.

Table 2. Trends in use of menopausal hormone therapy (estrogen only) among US women with hysterectomy, by age and race/ethnicity, 2000-2008

	NH White		NH Black		Hispanic	
	%	95% CI	%	95% CI	%	95% CI
Ages 50+						
2000	18.6	(17.4-19.8)	11.5	(9.1 - 14.3)	9.4	(7.1 - 12.4)
2005	9.0	(8.1 - 10.0)	6.1	(4.3 - 8.6)	5.6	(3.5 - 8.9)
2008	5.9	(5.1 - 6.8)	3.7	(2.4 - 5.7)	2.1	(1.1 - 4.2)
Ages 50-59						
2000	22.1	(20.0 - 24.3)	18.0	(13.7 - 23.2)	10.9	(7.4 - 15.7)
2005	9.0	(7.6 - 10.6)	8.1	(4.8 - 13.2)	4.3	(2.3 - 7.8)
2008	6.9	(5.5 - 8.5)	4.3	(2.6 - 7.2)	2.0	(0.7 - 5.8)
Ages 60-69						
2000	23.1	(20.7 - 25.6)	10.2	(6.9 - 14.7)	8.5	(5.2 - 13.7)
2005	12.6	(10.4 - 15.0)	7.3	(4.9 - 10.9)	10.0	(4.6 - 20.5)
2008	7.6	(5.8 - 9.8)	5.9	(3.0 - 11.2)	2.8	(1.0 - 8.0)
Ages 70+						
2000	11.6	(10.2 - 13.2)	2.6	(1.4 - 5.0)	8.1	(4.7 - 13.6)
2005	6.1	(5.0 - 7.6)	1.6	(0.7 - 3.7)	3.3	(1.3 - 8.1)
2008	3.3	(2.3 - 4.6)	0.2	(0.0 - 1.3)	1.7	(0.4 - 6.8)

Source: National Health Interview Survey.

Note: Survey questions from 2000 and 2005 are not directly comparable to 2008.

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