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Disparities in breast cancer survival in the United States (2001-2009): findings from the CONCORD-2 study

Running title: Breast cancer survival in the US by race and stage

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Keywords: Breast cancer; population-based survival; health disparities; trends

Precis: Breast cancer survival remained high from 2001 to 2009, but there were wide and persistent disparities in survival between black and white women. Reducing racial disparities in breast cancer survival remains a challenge that requires broad, coordinated efforts at the federal, state, and local levels.

ABSTRACT

Background: Reducing breast cancer incidence and achieving equity in breast cancer outcomes remains a priority for public health practitioners, health care providers, policy makers and health advocates. Monitoring breast cancer survival can help evaluate the effectiveness of health services, quantify inequities in outcomes between states or population sub-groups, and inform efforts to improve the effectiveness of cancer management and treatment.

Methods: We analyzed breast cancer survival using individual patient records from 37 statewide registries that participated in the CONCORD-2 study, covering approximately 80% of the US population. Women were diagnosed during 2001-2009 and followed up through December 31, 2009. We estimated age-standardized net survival at 1, 3 and 5 years after diagnosis, by state, race (white, black), stage at diagnosis, and calendar period (2001–2003 and 2004–2009).

Results: Overall, 5-year breast cancer net survival is very high (88.2%). Survival remained remarkably high from 2001 to 2009. During 2001–2003, survival was 89.1% for white women and 76.9% for black women. During 2004–2009, survival was 89.6% for white women and 78.4% for black women.

Conclusion: Breast cancer survival was more than 10 percentage points lower for black women than for white women and this difference persisted over time. Reducing racial disparities in survival remains a challenge that requires broad, coordinated efforts at the federal, state, and local levels. Monitoring trends in breast cancer survival can highlight populations in need of improved cancer management and treatment.

INTRODUCTION

The burden of breast cancer has been a persistent concern among public health practitioners, health care providers, policy makers, and health advocates. Worldwide, breast cancer is the second most common cancer and the fifth leading cause of cancer deaths among women.¹ In the United States, breast cancer is the most commonly diagnosed cancer (excluding skin cancer) and the second leading cause of cancer deaths among women.² Since early 2004, breast cancer incidence has been stable, while breast cancer mortality has been decreasing.³ But these changes have not been equal among all populations.³

Elimination of health disparities is a goal of many federal agencies. For example, the US Department of Health and Human Services, the Agency for Healthcare Research and Quality, and the Centers for Disease Control and Prevention have developed action plans to reduce health disparities.⁴⁻⁷ Unequal incidence of advanced-stage breast cancer, receipt of high-quality treatment and breast cancer death rates have not changed much over time.^{5,8} Breast cancer incidence rates have been higher among white women, but mortality rates have been higher among black women. The annual average percentage change (AAPC) in incidence from 1999–2013 varied by race; among white women there was a 0.8% decrease per year and a 0.4% increase per year among black women.⁹ Breast cancer mortality rates have fallen since the mid-1990s to 2012 among both black and white women, but the rate of decline has been faster among white women (APC -1.9% versus -1.5%).¹⁰⁻¹² Even though there have been great advancements in treatment options, racial inequalities in breast cancer survival in the United States still persist.

Evaluation of population-based survival trends can help to inform cancer control efforts by identifying opportunities for improvement in early detection, diagnosis, and treatment.

Population-based survival is a key measure of the effectiveness of cancer management and treatment.¹³ Black women are more often diagnosed with regional or late stage disease and have higher death rates than white women, regardless of stage.¹⁴ In 2008, the CONCORD study reported 5-year population-based survival in 31 countries, including 22 registries in 16 US states.¹⁵ Five-year survival in North America was among the highest in the world at 84.0%, with large survival differences between white (84.7%) and black (70.9%) women in the United States, suggesting that black women may not have the same access to and quality of care as white women. The second cycle of the CONCORD program (CONCORD-2) examined survival from 10 common cancers in 67 countries.¹⁶ CONCORD-2 is the largest study of population-based cancer survival trends to date, evaluating trends in 5-year survival for over 25 million individual patients diagnosed during the 15 years between 1995 and 2009. Age-standardized 5-year net survival from breast cancer increased in many countries world-wide. In the United States, it rose from 86.0% in 1995-99 to 88.6% in 2005-2009.

Using the US data from CONCORD-2, we examined the distribution of breast cancer stage at diagnosis by race, state, and over time. We also analyzed survival trends by race, stage, and state.

MATERIAL AND METHODS

Data

We used data from 37 state cancer registries funded by either the CDC's National Program of Cancer Registries, the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) program, or both. These registries participated in the CONCORD-2 study,¹⁷ covered approximately 80% of the US population. Registries consented to inclusion of their data in the more detailed analyses reported here. We analyzed individual tumor records for 1,372,377 women (aged 15-99) who were diagnosed with breast cancer (International Classification of Diseases for Oncology 3rd edition - ICD-O-3¹⁸ - C50.0-C50.6; C50.8-C50.9) during 2001-2009 and followed up to December 31, 2009. We included primary invasive cancers of the breast, regardless of whether the woman had a previous cancer. If a woman was diagnosed with two or more cancers of the breast during 2001 through 2009, only the first was considered in the survival analyses.

Patients were grouped by year of diagnosis into two calendar periods (2001-2003 and 2004-2009) to reflect changes in the methods used by US registries to collect data on stage at diagnosis. From 2001, most registries coded stage directly from the source data to SEER Summary Stage 2000 (SS2000).¹⁹ From 2004, all registries began to derive SS2000 using the Collaborative Staging System.²⁰

Survival analyses

We estimated net survival up to 5 years after diagnosis and 95% confidence intervals (CI) using the Pohar Perme estimator.²¹ We analyzed survival by race, stage at diagnosis, calendar period of diagnosis, and state. Net survival is the probability of survival up to a given time since diagnosis, after controlling for other causes of death (background mortality). To control for the

wide differences in background mortality among participating states, we constructed life tables of all-cause mortality in the general population of each state from the number of deaths and the population, by single year of age, sex, calendar year and, where possible, by race (black, white), using a flexible Poisson model.²² The life tables have been published.²³

We estimated net survival using the cohort approach for patients diagnosed in 2001-2003, since all patients had been followed up for at least five years by December 31, 2009. We used the complete approach to estimate net survival for patients diagnosed during 2004-2009, because 5 years of follow-up data were not available for all patients. Net survival was estimated for 5 age-groups (15-44, 45-54, 55-64, 65-74, and 75-99 years). We obtained age-standardized survival estimates using the International Cancer Survival Standard (ICSS) weights.²⁴ If two or more of the five age-specific estimates could not be obtained, we present only the pooled, unstandardized survival estimate for all ages combined. Trends, geographic variations, and differences in age-standardized survival by race are presented graphically in bar-charts and funnel plots.²⁵

More details on data and methods are provided in an the accompanying article.²⁶

RESULTS

There were 1,372,377 US women (85.1% white women and 10.4% black women) diagnosed with breast cancer in participating registries during 2001-2009. Overall there were no substantial changes in SEER Summary Stage distribution between 2001-2003 and 2004-2009 (Table 1). In 2001-2003, most breast cancers were diagnosed at local stage (61%). Around 30% of the cancers were regional stage and less than 5% were distant stage. The proportion of women with unknown stage was low at 7%. The distribution remained similar in 2004-2009, showing a slight

reduction of the percentage of cancers of unknown stage cancer. The stage distribution varied slightly between states (Supplement Table 1). In both 2001-2003 and 2004-2009, a lower proportion of black women were diagnosed at local stage, and the proportion of distant stage was about 1.6 times that of white women.

Survival decreased with time after diagnosis. Survival at 3 years was lower than at 1 year after diagnosis, and survival at 5 years was lower than at 3 years after diagnosis in both time periods (Table 2). In 2001-2003, breast cancer 5-year net survival for all races combined was high at 88.2% and remained so at 88.6% during 2004-2009. Overall, the difference in 5-year survival between black women and white women was more than 10 percentage points in 2001-2003 and this disparity did not decrease over time. In 2004-2009, survival varied widely between states (range: 85.4%-92.4%) and it was systematically lower for black women (Supplement Table 2).

Five-year net survival was high for women diagnosed with local stage cancer during 2001-2003 at 98% and remained high for women diagnosed during 2004-2009 (Table 3). In both time periods, the difference in survival between white women and black women was highest for regional (82.3% and 83.5% for white women vs. 69.9% and 71.8% for black women) and distant tumors (22.5% and 25.7% for white women vs. 15.2% and 17.1% for black women). This difference was noticed in all states and did not decrease over time (Supplement Table 3). For local stage, the racial disparity persisted but to a smaller extent (98.2% and 98.6% for white women vs. 92.8% and 94.3% for black women).

Figure 1 shows the 5-year age-standardized net survival by state. In 2001-2003, 5-year survival for breast cancer was very high at approximately 90%. Survival remained high in 2004-2009, with slight variation between states and regions. There was 0.5% increase in net survival across the United States. The change in survival among states ranged from -2.9% to 3.6%.

Figure 2 reports funnel plots of net survival for 2001-2003 and 2004-2009 to provide further insight into the variability of breast cancer survival in the United States by race and state. The plots show how much a particular survival estimate deviates from the pooled US value (the ‘target’, represented in the plot by the horizontal line) given the precision of each estimate.^{24,25} These plots show striking geographical and racial variation in survival. During 2001-2003 net survival was lower for black women in all states. Although survival for black women increased slightly during 2004-2009, survival remained lower for black women compared to white women in most states. In most states, survival for white women was above the pooled US estimate, while survival for all black women was below the pooled US estimate.

DISCUSSION

This study is the largest study on trends in population-based breast cancer survival in the United States. It is also unique in that the data are analyzed by race, stage at diagnosis, and state. This expands the US results from CONCORD-2, by providing detailed analysis of net survival by race and stage at diagnosis. Population-based survival is a key measure of the overall effectiveness of the health system in dealing with cancer and therefore is a useful measure for

evaluating access to and quality of care and appropriate treatment. These results can be used to plan future cancer control strategies.

Overall, survival for breast cancer was strikingly high in 2001-2003 and remained high during 2004-2009. There was wide variability in survival between states, with lower survival for black women than white women in all 37 states included in the analyses. Disappointingly, the more than 10% difference in survival between white and black women did not improve over time. More efforts need to be initiated to understand the reasons for this persistent racial disparity in breast cancer survival and to help black women in accessing early diagnosis and appropriate treatment.

Black/white inequalities in survival suggest differences in access to care and differences in tumor morphology between the groups. With the same stage of disease, net survival is lower among black women. However, black/white differences in mammography rates by state are not consistent with stage of disease or survival. In fact, there are no significant state-specific differences between black and white women who report having had a mammogram within the past two years during the study periods.²⁷

Clinical perspective

Having access to diagnostic studies and high quality treatment is important for improving breast cancer survival. Black women are more likely than white women to experience delays in

treatment and not receive appropriate treatment for breast cancer.²⁸ Delays in care and inappropriate treatment can result in larger tumors and poorer outcomes. Timely follow-up of abnormal test results and receipt of treatment after diagnosis could improve outcomes of all women with breast cancer.²⁹ Access to quality care is a key factor to reducing disparities in breast cancer survival.

Breast cancer is a very heterogeneous disease. There are several different types of breast cancer with multiple sub-types based upon biomarkers such as estrogen receptor, progesterone receptor, and human epidermal growth factor receptor status. Differences in tumor morphology not only dictate treatment but also are prognostic. For example, triple negative breast cancer (breast cancer subtype that does not have estrogen and progesterone receptors or HER2 protein) is a more aggressive tumor with lower survival that is more often diagnosed among black women.^{30,31} There may be other tumor characteristics or underlying biologic differences between black and white women impacting tumor progression or therapy response that could be contributing to the observed survival differences by race.

Research is continually identifying new tumor biomarkers that have potential for use in a clinical setting. As treatment becomes more individualized, not all options are always available to all patients. Therefore, as newer treatments improve survival, it may not improve survival among all women equally. If minority or low-income women do not have access to newer treatment options, survival improvements may not be as apparent among these groups in population-based

surveillance systems. This may be one reason we see that at the same stage of diagnosis, net survival is lower among black women than among whites.

Cancer Control perspective

In addition to addressing potential racial differences in the clinical care for breast cancer to reduce racial breast cancer survival disparities, there are several health behavior factors that can reduce risk for breast cancer.³²⁻³⁵ Modifying risk factors such as obesity, lack of physical activity, alcohol consumption, exposure to environmental toxins, and use of hormonal therapy can reduce a woman's risk of getting breast cancer. Black women often have more co-morbid conditions which put them at greater risk for poorer survival outcomes.³⁶ For women who may be at high risk for breast cancer due to family history or genetic reasons, they may need enhanced screening and risk reduction procedures such as taking antiestrogens or having prophylactic mastectomy. Minority and low-income women more often have limited access to these options^{37,38} which ultimately may put them at increased risk of dying from breast cancer.

Once diagnosed with breast cancer, women need to be educated and empowered to take part in treatment decisions and to receive timely, guideline-concordant, and complete treatment. Women who have lack of trust in the health care system or who are characterized by cultural differences from their health care providers, may not get the needed treatment and supportive care.³⁹ Studies that analyzed the availability of equal treatment among all patients found that patient have similar outcomes when they receive equal treatment.⁴⁰⁻⁴³ This suggests that the large and persistent survival deficit in black women during 2001-2009 may be attributable to receipt of less

effective treatment. Supportive care is also an area that needs more attention. Specifically, interventions to address geographical isolation, cultural differences, financial burden, and fear may be needed to improve access to quality care. These issues may be addressed along with clinical care.

Strengths and Limitations

This is the largest study comparing breast cancer survival by state and race using data from CONCORD-2 which includes high-quality data covering more than 80% of the US population. In addition, for women diagnosed with breast cancer, 98.9% of cases were morphologically verified, and the percentage of cases with unknown stage was low.⁴⁴ All the participating registries were certified by the North American Association of Central Cancer Registries as having met data quality and completeness standards (<http://www.naaccr.org/Certification/Criteria.aspx>).

This study had a few limitations. First, the follow-up procedures in the United States differed according to the federal funding source.⁴⁵ All SEER registries are required to conduct follow-up of all cases to ascertain vital status. NPCR registries are only funded to ascertain deaths through linkage with the state vital records and the National Death Index. Second, the manner in which SEER Summary Stage 2000 data were collected and reported changed for all registries in 2004 as described in the methods section. This resulted in the percentage of unknown stage cases decreasing when stage was derived rather than manually coded. Some state cancer registries assumed a case to be alive if the case was not included on state death certificate databases or on

the National Death Index. Next, the states in the Western Region (Mountain and Pacific Divisions) have too few black women to reliably assess racial differences and some states did not report stage data which could result in the data not being generalizable to the entire United States. Finally, vital status follow-up data was only available through December 31, 2009. Therefore, we did not have 5-year follow-up for each patient.

Conclusion

There is increasing awareness and effort to achieve health equity among racial, ethnic, geographic, socioeconomic, and other groups. With the persistent disparity in breast cancer survival between black women and white women, more national, local, and individual efforts are needed. This study provides accurate, useful information on incidence and survival of breast cancer patients in various US subpopulations and is supported through a nation-wide system of central cancer registries funded by CDC's NPCR or NCI's SEER program.⁴⁵

CDC and its partners are dedicated to identifying and addressing the factors that lead to health disparities among racial, ethnic, geographic, socioeconomic, and other groups so that barriers to health equity can be removed. CDC's National Breast and Cervical Cancer Early Detection Program works with the states, tribes/tribal organizations, and territories to provide assistance to low-income women to ensure that they have access to appropriate breast and cervical cancer screening, diagnostic, and treatment services.⁴⁵ The CDC's Comprehensive Cancer Control Program works with states, tribes/tribal programs, and territories to develop cancer control plans that focus on prevention, screening, and survivorship issues.⁴⁵ Working with partner

organizations such as the National African American Tobacco Prevention Network and the National Alliance for Hispanic Health, these programs target specific populations who are at risk of developing or dying from cancer.

Eliminating or reducing disparities in breast cancer survival will require broad, coordinated population efforts at various federal, state, and local levels. The persistent black/white disparities in breast cancer survival reported here demonstrate that increased focus on individual, provider, community, organizational, and policy levels are warranted. Public health has an important opportunity to expand outreach to medically underserved women, provide education about breast cancer risk reduction, and increase awareness about post-treatment strategies to improve outcomes. Evidence-based interventions to further improve provider awareness, knowledge and practice need to also be identified. Finally, public health professionals can champion community-level engagement and partnerships to leverage organizational infrastructure and provide evidence to inform organizational policies to ensure equal cancer care among all women and reduction in breast cancer survival disparities. Focusing on education and informed decisions, cultural sensitivities, personalized care, and equal access to care are critical steps.

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Tables and Figures

Table 1. Breast cancer: number of cases for females (aged 15-99 years) diagnosed 2001-2003 and 2004-2009 and distribution (%) by SEER Summary Stage 2000 at diagnosis, by race and calendar period of diagnosis.

Table 2. Breast cancer: age-standardized net survival (%) at 1-, 3- and 5-years for females (aged 15-99 years) diagnosed 2001-2009, by race and calendar period of diagnosis.

Table 3. Breast cancer: 5-year age-standardized net survival (%) for females (aged 15-99 years) diagnosed 2001-2003 and 2004-2009, by SEER Summary Stage at diagnosis, race, and calendar period of diagnosis.

Figure 1. Breast cancer: 5-year age-standardized net survival (%) for adult females (aged 15-99 years) diagnosed during 2001-2003 and 2004-2009, and absolute change (%): states grouped by US Census Region.

Note: Data from 37 statewide cancer registries (covering 80.6% of the population) are ranked within US Census Region by the survival estimate for 2004-2009. Dark colors denote states funded by CDC's National Program of Cancer Registries (NPCR); pale colors denote states funded by NCI's Surveillance, Epidemiology and End Results (SEER) Program; * denotes states funded by both federal surveillance programs. Change (%) not plotted if a survival estimate was not available for one calendar period or one or more estimates was not age-standardized.

Figure 2. Breast cancer: 5-year age-standardized net survival (%) for adult females (aged 15-99 years), by state, race and calendar period of diagnosis.

Note: the pooled (US) survival estimate for each calendar period is shown by the horizontal (solid) line with corresponding 95.0% and 99.8% control limits (dotted lines).

Supplement Table 1. Breast cancer: number of cases for females (15-99 years) diagnosed 2001-2009 and distribution (%) by SEER Summary Stage 2000 at diagnosis, by race, calendar period of diagnosis, and US Census Region and States.

Note: NPCR indicates National Program of Cancer Registries; SEER indicates Surveillance, Epidemiology, and End Results program. Information on stage was not available for two states (Maryland and Wisconsin), or for Rhode Island for cases diagnosed during 2004- 2009.

Supplement Table 2. Breast cancer: age-standardized net survival (%) at 1-, 3- and 5-years for females (15-99 years) diagnosed 2001-2009, by race, calendar period of diagnosis, and US Census Region and States.

Note: NPCR indicates National Program of Cancer Registries; SEER indicates Surveillance, Epidemiology, and End Results program. Unstandardized estimates are italicized.

Supplement Table 3. Breast cancer: 5-year age-standardized net survival (%) for females (15-99 years) diagnosed 2001-2009, by SEER Summary Stage 2000 at diagnosis, race, calendar period of diagnosis and US Census Region and States.

Note: NPCR indicates National Program of Cancer Registries; SEER indicates Surveillance, Epidemiology, and End Results program. Information on stage was not available for two states (Maryland and Wisconsin), or for Rhode Island for cases diagnosed during 2004- 2009. Unstandardized estimates are italicized.

Table 1. Breast cancer: number of cases for females (aged 15-99 years) diagnosed 2001-2003 and 2004-2009 and distribution (%) by SEER Summary Stage 2000 at diagnosis, by race and calendar period of diagnosis.

SS2000	2001-2003			2004-2009			
		All races	White	Black	All races	White	Black
No. of patients		446,106	385,888	42,401	926,271	782,220	100,611
Local	(%)	59.1	60.5	47.5	59.1	60.5	48.5
Regional	(%)	29.8	29.1	35.3	30.2	29.6	35.2
Distant	(%)	4.4	4.2	6.8	5.2	4.9	7.8
Unknown	(%)	6.7	6.2	10.3	5.4	5.0	8.4

Table 2. Breast cancer: age-standardized net survival (%) at 1-, 3- and 5-years for females (aged 15-99 years) diagnosed 2001-2009, by race and calendar period of diagnosis.

Years	2001-2003									2004-2009														
	All races			White			Black			All races			White			Black								
	NS (%)	95% CI		NS (%)	95% CI		NS (%)	95% CI		NS (%)	95% CI		NS (%)	95% CI		NS (%)	95% CI							
1	96.5	96.4	-	96.6	96.8	96.7	-	96.9	92.6	92.2	-	93.0	96.7	96.7	-	96.8	97.0	97.0	-	97.1	93.6	93.3	-	93.8
3	91.8	91.6	-	91.9	92.5	92.4	-	92.7	83.1	82.5	-	83.7	92.1	92.0	-	92.2	92.9	92.7	-	93.0	84.3	83.9	-	84.8
5	88.2	88.0	-	88.3	89.1	88.9	-	89.3	76.9	76.2	-	77.6	88.6	88.4	-	88.8	89.6	89.4	-	89.8	78.4	77.7	-	79.1

Table 3. Breast cancer: 5-year age-standardized net survival (%) for females (aged 15-99 years) diagnosed 2001-2003 and 2004-2009, by SEER Summary Stage at diagnosis, race, and calendar period of diagnosis.

SS2000	2001-2003												2004-2009											
	All races				White				Black				All races				White				Black			
	NS (%)	95% CI			NS (%)	95% CI			NS (%)	95% CI			NS (%)	95% CI			NS (%)	95% CI			NS (%)	95% CI		
All stages	88.2	88.0	-	88.3	89.1	88.9	-	89.3	76.9	76.2	-	77.6	88.6	88.4	-	88.8	89.6	89.4	-	89.8	78.4	77.7	-	79.1
Local	98.0	97.8	-	98.2	98.2	98.0	-	98.4	92.8	91.9	-	93.7	98.3	98.1	-	98.6	98.6	98.3	-	98.8	94.3	93.4	-	95.2
Regional	81.2	80.8	-	81.6	82.3	82.0	-	82.7	69.9	68.5	-	71.2	82.3	81.9	-	82.7	83.5	83.0	-	83.9	71.8	70.4	-	73.2
Distant	21.5	20.9	-	22.2	22.5	21.7	-	23.2	15.2	13.6	-	16.9	24.5	23.7	-	25.2	25.7	24.9	-	26.6	17.1	15.4	-	18.8
Unknown	72.5	71.8	-	73.2	73.1	72.4	-	73.9	65.9	63.8	-	67.9	72.6	71.9	-	73.4	73.2	72.4	-	74.1	68.3	66.3	-	70.4