Male breast cancer: are there racial disparities in incidence and tumor characteristics?

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Abstract:

Background: Racial disparities in female breast cancer (BC) outcomes have been well documented; however, less is known about patterns of BC and outcome disparities in men.

Methods: Data (1973 to 2012) from the Surveillance, Epidemiology, and End Results Program database were used to compare BC patterns among Non-Hispanic Black (NHB) and Non-Hispanic White (NHW) men and women. Differences in tumor characteristics analyzed included estrogen receptor (ER), progesterone receptor (PR) status, stage and grade.

Results: BC incidence was 1.00 per 100,000 for men and 116.21 for females. Among men, the BC incidence was 51% higher for NHB compared to NHW (rate ratio = 1.51, 95% CI: 1.42 – 1.61). Men were diagnosed an average of 5 years later than women; however NHB men (average age at diagnosis 63 years) overall were diagnosed 4 years earlier than NHW men (average age at diagnosis 67 years). NHB men showed a higher proportion of ER negative tumors compared to NHW men. As compared to NHW men, the odds of NHB men developing ER- BC was 1.67 (95% CI [1.21 – 2.31]) and 1.84 for ERPR- (95% CI [1.28 – 2.67]).

Conclusion: As observed among NHB women, NHB men are more likely to be diagnosed with more advanced disease features and also experience a higher proportion of hormone negative BC compared to NHW men.

1. Background:

Male breast cancer (BC) is a relatively uncommon form of cancer with an estimated 2,600 new cases in the United States in 2016. This number is dwarfed by the occurrence of female BC (246,660 new cases in the same year) (1). Due to its rare incidence, male BC has received considerably less attention compared to female BC. Prior studies that have compared breast cancer incidence and outcomes between men and women have shown that while the incidence for men is much lower (approximately 1.1 per 100,000 person-years), (2) mortality after diagnosis is considerably higher. Indeed, men diagnosed with BC are 27% more likely to die from the disease as compared to their female counterparts. From 1973 to 2005, men have had a slower decline in BC mortality; 28% as compared to 42% for women (2, 3). Men also present with lower grade and more estrogen receptor positive BC and were older at diagnosis (2). An earlier study over a limited time period (1991-2002) restricted to men over the age of 65 with stage 1-3 breast cancer and a much smaller sample size (456 white men and 34 black men) reported racial disparities in treatment and survival (2, 4). The present study extends this earlier work over a longer time frame without age restrictions and compares the pattern of the disease by and within gender and ethnicity.

It is well established that Non-Hispanic Black (NHB) women, while somewhat less likely to be diagnosed with BC, are more likely than their Non-Hispanic White (NHW) women counterparts to be diagnosed at a later stage. They (NHB women) also present with tumor characteristics indicating more aggressive disease, including tumors lacking estrogen and progesterone receptors and Human Epidermal Growth Factor Receptor 2 (ER - ,PR- and Her2-); the so-called triple negative BC (TNBC). Among women, NHB patients are subsequently more likely to experience lower survival and higher BC mortality rates when compared to NHW women (5). Female BC mortality disparities appear to be more pronounced for younger and pre-menopausal women whose incidence is actually higher for NHB compared to NHW women (6). While racial disparities in female BC have been studied extensively and are well documented, less is known about tumor characteristics and survival associated with male BC, including racial disparities among males.

The Surveillance, Epidemiology, and End Results (SEER) Program data have been previously used to report racial disparity in males affected by BC or to compare male BC to female BC (2, 4). However, few studies have investigated similarities in BC among NHB men and NHB women. Using the SEER database for wider coverage including recent years (1973-2012), we are exploring and documenting racial and gender disparities in BC without age restrictions with an emphasis on existing similarities among NHB men and women.

2. Materials and Methods:

Data and population

Data from 1973 to 2012 from the Surveillance, Epidemiology, and End Results Program (SEER) database (7) were used to estimate the incidence, distribution of tumor characteristics and survival by race (NHW and NHB) and gender. The SEER database includes 20 registries that represent about 28% of the geographic area of the USA (8). Due to Hurricane Katrina, data from Louisiana in 2005 were excluded from the analysis of incidence and tumor characteristics, but were included in survival analyses.

Statistical Analysis and Modeling

BC incidence

Age-standardized incidence rates (ASR) were adjusted to the 2000 US-standard population by five year age groups and calculated by direct standardization. Population denominators and Person-years (P-years) were derived from US Census Bureau estimations obtained from SEER. Instead of expressing the age specific rate per 100,000, the age-specific burden modeling (that has been described and discussed extensively in our previous work on breast or endometrium cancers among NHB and NHW in the USA) was used (6, 9). Briefly, population structures between NHB and NHW showed strong differences. Therefore, we modeled the expected number of cases in a standard population in which the observed age-specific rates are adjusted to the world-standard population. This approach minimized the tendency to overestimate cancer burden in older age groups (where the denominator is low) and thus provided a more accurate distribution of cancer burden across different age groups. In secondary analyses we estimated incidence using the 2000 US standard population. Rate ratios (RR) and 95% confidence intervals (CI) were calculated separately for men and women, and separately for NHB and NHW individuals by gender and were further stratified by age group (<50 vs. 50 years and above). Analyses were conducted using Stata version 14 (StataCorp. 2015. Stata Statistical Software: Release 14. College Station, TX: StataCorp LP.).

Distribution of tumor characteristics

Distributions of age at diagnosis were compared within racial and gender groups and t-tests were employed to assess statistical differences. The distributions of stage at diagnosis, tumor grade, ER, PR, and ERPR status were tabulated by gender, by race (within gender), and by age group (<50 and 50 and above) within race and gender groups, and Pvalues from chi-square tests (with an alpha at 0.05) of association were used to assess statistical differences. We used marginal standardization (predictive margins) using the margins command in Stata to estimate adjusted prevalence and prevalence differences. A logistic regression model was used to estimate the odds ratio (OR) of NHB to develop and ER negative (ER-) and ERPR negative (ER-PR-) BC. The models were adjusted for age, tumor grade, stage, calendar year and SEER registries. SEER started to collect information on HER2 status in 2010; therefore this information was missing from 1973 to 2009 and was available for 12 to 15% of the patients of the study. The ER and PR status was known for at least 65% of the patients as SEER started to collect this information in 1990. Therefore, due to the low number of cases, the distribution of HER2 status and BC subtypes were not reported by age group; their odds ratio and survival were also not provided.

Survival analysis

Survival analyses were conducted using SEER*Stat 8.2.1 (10) (Database: Incidence - SEER 18 Registry Research Data and Hurricane Katrina Impacted Louisiana Cases, from the November 2013 submission (2000-2012) with the Katrina/Rita Population Adjustment) by gender and ethnicity. These analyses were restricted to cases with the ER and PR status was available.

3. Results:

Incidence by gender and race

From 1973 to 2012, 1,147 and 7,108 BC cases were identified among NHB and NHW men, respectively; and 126,673 and 1,041,145 BC cases were identified among NHB and NHW women, respectively. The ASR was 1.00 per 10^5 P-years for men and 116.21 per 10^5 P-years for females. BC incidence was 51% higher in NHB men (1.44 per 10^5 P-years) compared to NHW men (0.95 per 10^5 P-years) with a corresponding rate ratio (RR) of 1.51 (95% CI: 1.42 – 1.61). In contrast, BC incidence was lower for NHB women (107.95 per 10^5 P-years) compared to NHW women (115.25 per 10^5 P-years) over the years examined with a corresponding rate ratio RR = 0.94 (95% CI: 0.93 – 0.94). Incidence was higher for NHB men compared to NHW males across all age groups (no crossover observed) and has remained so for more than 20 years (Figure 1 and 2). In contrast, a clear convergence in BC incidence is observed among NHB and NHW women; in 2012 the ASR was 119.83 per 10^5 P-years for NHB women vs. 114.72 per 10^5 P-years for NHW women.

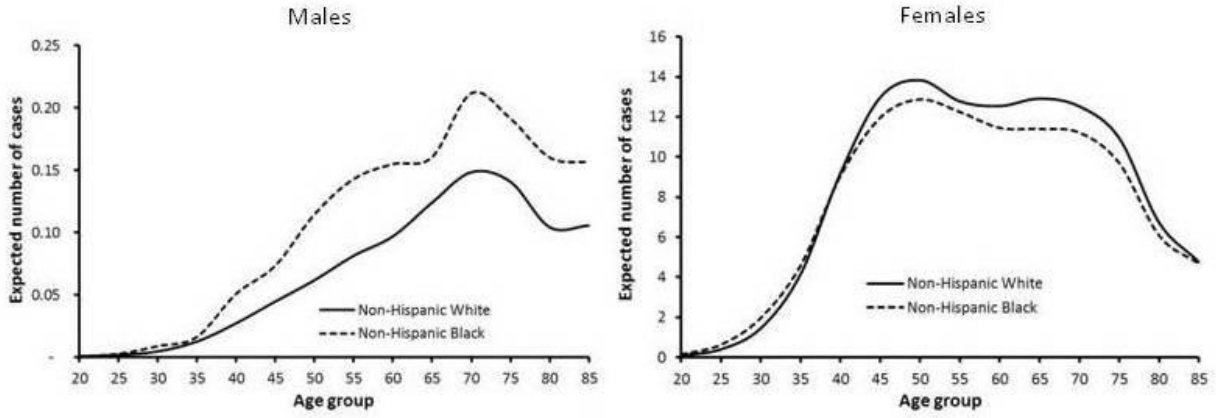

Figure 1: Distribution of breast cancer burden (expected number of cases) by gender and race/ethnicity. Estimations are based on observed age-specific incidence rates and the 2000 US-standard population.

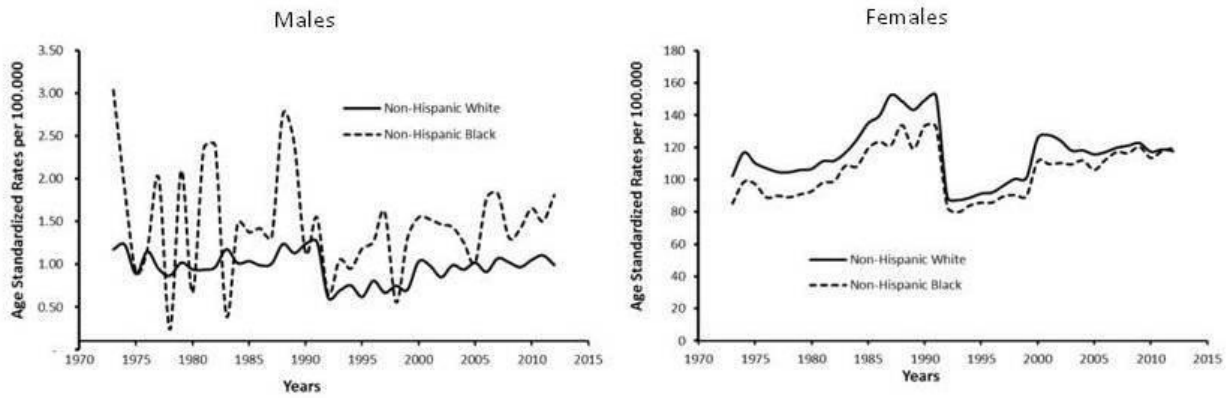

Figure 2: Breast cancer age standardized rate (ASR) adjusted to the 2000 US-standard population over the years and by gender and race/ethnicity.

Trends in incidence by age at diagnosis

Men were diagnosed an average of 5 years (95% CI: 4.26 – 4.87) later than women (67 vs. 62 years, respectively). Regardless of gender, NHB individuals were more likely to be diagnosed at a younger age: NHB women were diagnosed an average of 4 years (95% CI: 3.98 – 4.15) earlier than NHW women (58 vs. 62 years); likewise, NHB men were diagnosed an average of 4 years (95% CI: 3.11 – 4.71) earlier than NHW men (63 vs. 67 years).

Tumor characteristics by gender and race

The proportion of tumors diagnosed as *in*-situ was lower in men than women and no racial disparity was evident among men. Whereas NHW women tended to be diagnosed with better differentiated (lower grade) tumors than NHB women, no racial difference in the distribution of tumor grade was apparent for men. Men tended to be diagnosed at a later stage than women. Respectively 49% and 46% (Pvalue <0.05) of NHB and NHW men were diagnosed with regional or distant stage, compared with 37% and 30% (Pvalue <0.05) of NHB and NHW women. NHB men had a higher prevalence of distant metastatic BC compared to NHW men (11% as vs. 7%, respectively Pvalue <0.05) (Table 1).

The proportion of BC lacking ER and or PR expression (ER- and or PR-) was considerably lower for men compared to women (5% vs. 20%, Pvalue <0.05 for ER- and 15% vs. 31%, Pvalue <0.05 for PR-) (Table 1). Similarly to NHB women who have shown a higher proportion of ER negative (ER-) BC compared to NHW women (32% vs. 19%, PD=0.08, (95% CI [0.08 - 0.09]), the prevalence of ER- BC was higher for NHB men compared to NHW men (8% vs 5% P <0.05 Prevalence Difference (PD) =0.03, (95% CI [0.01 - 0.06]). NHB males had a higher proportion of PR- BC as compared to NHW males. Overall, NHB individuals showed a higher proportion of ER-PR- BC as compared to NHW individuals; 8% vs. 4% (Pvalue <0.05) for men and 36% vs. 20% (Pvalue <0.05) for women. Compared to NHW persons, the odds ratio (OR) to develop ER- BC was 1.62 (95% CI [1.17 – 2.24]) for NHB men and 1.72 (95% CI [1.69 – 1.75]) for NHB women. With regard to ER-PR- BC, NHB men had an OR of 1.80 (95% CI [1.24 – 2.59]) and NHB women an OR of 1.83 (95% CI [1.79 – 1.86]) compared to respectively NHW men and NHW women. Interestingly, men had a slightly higher proportion of HER2 negative BC as compared to females, but no difference between NHB and NHW men was observed (Table1). With regard to BC subtypes, Luminal A subtype was predominant among men and women. However, among men, the number with a reported BC subtype was too low to draw any conclusions with regard to race. Among women, NHB females had a higher proportion of triple negative BC compared to NHW women (21% vs. 10% Pvalue <0.05, Table 1).

The racial disparity in ER- negative and ER-PR- BC was mostly confined to older men, but evident for both younger and older female patients (Table 2). Among younger women (<50), the disparity in the distribution of ER negative BC was 14 percentage points higher for NHB as compared to NHW (39% vs. 25%, Pvalue <0.05), for ER-PR- BC it was 17 percentage points higher (42% vs. 25%, Pvalue <0.05) compared to NHW women. For older women, the disparity in ER- BC was 12 percentage points higher for NHB women (29% vs. 17%, Pvalue <0.05); it was 14 percentage points higher for ER-PR- BC (33% vs. 19%, Pvalue <0.05). In contrast, for men, the disparity was only

statistically apparent in the older age group (≥50) where NHB men had a higher proportion of ER- and ER-PR- as compared to NHW men; 8% vs. 5%, (Pvalue <0.05) for ER- and 7% vs. 4% (Pvalue <0.05)) for ER-PR- (Table 2). The same patterns were observed for PR negative BC with NHB men and women having a higher proportion of PR negative BC.

Survival by gender and race

Overall, survival at 5 years was lower for men compared to women (69% vs. 82% P <0.05) (Figure 3, Table S.1). Racial disparities in BC survival were apparent for both NHB and NHW males (63% vs. 72% P <0.05) and NHB and NHW female patients (73% vs. 83% P <0.05). Among men with ER negative BC, the 60 months survival was 56% for NHB compared to 63% for NHW patients (Pvalue>0.05). Among women it was of 65% for NHB compared to 73% for NHW patients (Pvalue<0.05) (Figure 3, Table S.1).

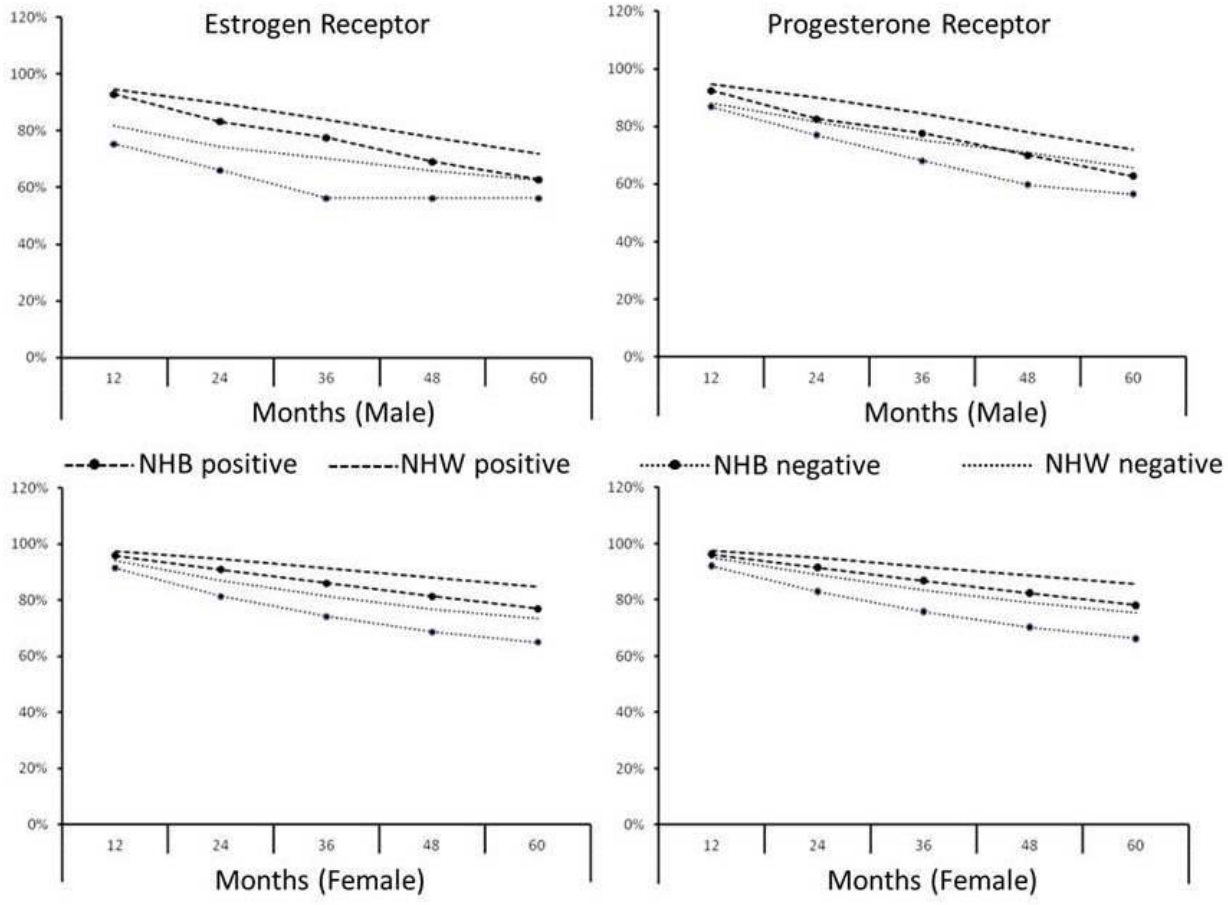

Figure 3: Breast cancer survival by gender, race/ethnicity according to the hormone receptor status.

4. Discussion:

The etiology of male BC is unclear and risk factors remain under studied. Established risk factors include a history of testicular abnormalities, radiation exposure, Klinefelter syndrome, benign breast conditions, high body mass index, hormone exposure, family history of BC, and BRCA2 mutations (11). Family history of male BC is considered to be a sign of genetic predisposition to female BC; it is more often related to the presence of BRCA2 mutation and is associated with an earlier age of onset (12, 13). People carrying a genetic predisposition are more likely to develop the disease at a younger age. Men who inherit a mutation in the BRCA2 gene have a 6% risk of developing BC by the age of 70 (14, 15). Though the proportion of male BC attributable to BRCA mutations is not established, population-based studies reported that young NHB women were more likely to harbor BRCA1/2 mutations compared to other ethnic groups (16.7% vs. 7.2% for NHW women of <35 years of age) (16, 17). The tendency for NHB women to be diagnosed at younger ages could reflect either a higher genetic predisposition to BC or a lower life expectancy as compared to NHW women. However, a study has shown that as compared to NHW women, NHB women affected by cancer were more likely to be diagnosed at a younger age and this was true even after the adjustment for the population structure (18). Furthermore, although there is a paucity of genetic studies among men of African Ancestry with regard to BC, it has been reported that the proportion of male BC among African men is among the highest and represents about 6% of all the cancers (19, 20).

The higher prevalence of hormone positive BC among men as compared to females has been reported previously (2, 21) and is confirmed in the present study. However to our knowledge, we are the first to report, the greater proportion of hormone negative BC among NHB men as compared to NHW men and to show how the profile of BC among NHB men is similar to that of NHB women in terms of tumor aggressivity patterns.

The greater prevalence of ER negative BC for NHB vs. NHW women is well established and has been associated with racial differences in parity, reproductive timing and socioeconomic status (22, 23). ER negative BC is more prevalent for women diagnosed at younger ages, but this proportion is still significantly higher among older NHB women compared to NHW women. With regard to men, one of the reasons why the disparity may be confined to older men is that men are more likely to be diagnosed at an older age and the number of cases in younger age men is still very small. It is likely that with a larger sample size that same disparity would be evident regardless of age. Furthermore, the patterns observed for PR- BC appears to more closely parallel the story in females with just a difference of 1% in the two age groups. The higher proportion of ER negative BC among women of <50 reinforces the need for adapted screening guidelines for women in their forties, but also the need for specific guidelines for hormone negative BC that's disproportionally affects NHB (both men and women) and a strategy for breast cancer awareness and early detection among men.

The different distribution of ER negative BC by gender is likely related to different factors driving this prevalence by gender. Among women ER and PR status are likely influenced by specific hormonal and reproductive factors including age at menarche and menopause, parity, breastfeeding and related factors (23), all of which are generally absent among men.

Given the lower prevalence of more aggressive and less treatable ER negative BC among men, we might anticipate better survival for men than for women. In the present study, the opposite was true: men diagnosed with BC experienced lower survival than women for both NHB and NHW. It has been reported that female BC subtypes do not give the same prognostic information for male BC even in ER and PR positive groups (24). Male BC has been found to harbor less somatic genetic alterations typically found in ER-positive/HER2-negative BC among females (25) and some results have suggested less efficacy with aromatase inhibitors and an increase in mortality risk compared to tamoxifen (13). Nevertheless, a multidisciplinary meeting focusing on differences and similarities between breast cancer in males and females and held by representatives from the fields of epidemiology, genetics, pathology and molecular biology, health services research, and clinical oncology and the advocacy community came to the conclusion that male breast cancer seems to resemble postmenopausal hormone receptor–positive disease in women (21).

5. Conclusion:

Due to the very rare occurrence of male BC in the United States, it is not surprising that the disease receives very little research or public health attention, with no screening guidelines and little research into prevention, early detection, or treatment. Men are not encouraged to "know their breasts" and changes may go unnoticed or not be brought to a health professional's attention leading to advancement of the disease and subsequent poorer survival. Greater attention should be paid to increasing early detection for men with a strong family history of BC or who have a female relative known to carry a BRCA 1 or 2 mutations. For these men, lifetime risk of breast cancer approaches that for women at average risk of BC for whom public health strategies are well established.

Reference

1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2016. CA: a cancer journal for clinicians. 2016;66(1):7-30. Epub 2016/01/09. doi: 10.3322/caac.21332. PubMed PMID: 26742998.

2. Anderson WF, Jatoi I, Tse J, Rosenberg PS. Male breast cancer: a population-based comparison with female breast cancer. Journal of clinical oncology : official journal of the American Society of Clinical Oncology. 2010;28(2):232-9. Epub 2009/12/10. doi: 10.1200/jco.2009.23.8162. PubMed PMID: 19996029; PubMed Central PMCID: PMCPmc2815713.

3. Miao H, Verkooijen HM, Chia KS, Bouchardy C, Pukkala E, Laronningen S, et al. Incidence and outcome of male breast cancer: an international population-based study. Journal of clinical oncology : official journal of the American Society of Clinical Oncology. 2011;29(33):4381-6. Epub 2011/10/05. doi: 10.1200/jco.2011.36.8902. PubMed PMID: 21969512.

4. Crew KD, Neugut AI, Wang X, Jacobson JS, Grann VR, Raptis G, et al. Racial disparities in treatment and survival of male breast cancer. Journal of clinical oncology : official journal of the American Society of Clinical Oncology. 2007;25(9):1089-98. Epub 2007/03/21. doi: 10.1200/jco.2006.09.1710. PubMed PMID: 17369572.

5. DeSantis CE, Fedewa SA, Goding Sauer A, Kramer JL, Smith RA, Jemal A. Breast cancer statistics, 2015: Convergence of incidence rates between black and white women. CA: a cancer journal for clinicians. 2016;66(1):31-42. Epub 2015/10/30. doi: 10.3322/caac.21320. PubMed PMID: 26513636.

6. Sighoko D, Fackenthal JD, Hainaut P. Changes in the pattern of breast cancer burden among African American women: evidence based on 29 states and District of Columbia during 1998 to 2010. Annals of epidemiology. 2015;25(1):15-25.e10. Epub 2014/12/03. doi: 10.1016/j.annepidem. 2014.09.006. PubMed PMID: 25442056.

7. http://seer.cancer.gov/registries/list.html.

8. http://seer.cancer.gov/about/overview.html.

9. Sighoko D. Ethnic and geographic variations in corpus uteri cancer burden: evidence based on data from 29 states and the District of Columbia. CI5 IX, X and SEER data (1998-2010). Cancer causes & control : CCC. 2014;25(9):1197-209. Epub 2014/07/06. doi: 10.1007/s10552-014-0425-z. PubMed PMID: 24989841.

10. ssp://seerstat.imsweb.com:2038.

11. Brinton LA, Cook MB, McCormack V, Johnson KC, Olsson H, Casagrande JT, et al. Anthropometric and hormonal risk factors for male breast cancer: male breast cancer pooling project results. Journal of the National Cancer Institute. 2014;106(3):djt465. Epub 2014/02/21. doi: 10.1093/jnci/djt465. PubMed PMID: 24552677; PubMed Central PMCID: PMCPmc3975166.

12. Riahi A, Ghourabi ME, Fourati A, Chaabouni-Bouhamed H. Family history predictors of BRCA1/BRCA2 mutation status among Tunisian breast/ovarian cancer families. Breast cancer (Tokyo, Japan). 2016. Epub 2016/03/31. doi:

10.1007/s12282-016-0693-4. PubMed PMID: 27025497.

13. Fentiman IS. Male breast cancer is not congruent with the female disease. Critical reviews in oncology/hematology. 2016. Epub 2016/03/19. doi: 10.1016/j.critrevonc.2016.02.017. PubMed PMID: 26989051.

14. Basham VM, Lipscombe JM, Ward JM, Gayther SA, Ponder BA, Easton DF, et al. BRCA1 and BRCA2 mutations in a population-based study of male breast cancer. Breast cancer research : BCR. 2002;4(1):R2. Epub 2002/03/07. PubMed PMID: 11879560; PubMed Central PMCID: PMCPmc83848.

15. Wolpert N, Warner E, Seminsky MF, Futreal A, Narod SA. Prevalence of BRCA1 and BRCA2 mutations in male breast cancer patients in Canada. Clinical breast cancer. 2000;1(1):57-63; discussion 4-5. Epub 2002/03/20. doi: 10.3816/CBC.2000.n.005. PubMed PMID: 11899391.

16. John EM, Miron A, Gong G, Phipps AI, Felberg A, Li FP, et al. Prevalence of pathogenic BRCA1 mutation carriers in 5 US racial/ethnic groups. Jama. 2007;298(24):2869-76. Epub 2007/12/27. doi: 10.1001/jama.298.24.2869. PubMed PMID: 18159056.

17. Pal T, Bonner D, Cragun D, Monteiro AN, Phelan C, Servais L, et al. A high frequency of BRCA mutations in young black women with breast cancer residing in Florida. Cancer. 2015;121(23):4173-80. Epub 2015/08/20. doi: 10.1002/cncr.29645. PubMed PMID: 26287763; PubMed Central PMCID: PMCPmc4666784.

18. Robbins HA, Engels EA, Pfeiffer RM, Shiels MS. Age at cancer diagnosis for blacks compared with whites in the United States. Journal of the National Cancer Institute. 2015;107(3). Epub 2015/02/02. doi: 10.1093/jnci/dju489. PubMed PMID: 25638255; PubMed Central PMCID: PMCPmc4326308.

19. Amir H, Makwaya CK, Moshiro C, Kwesigabo G. Carcinoma of the male breast: a sexually transmitted disease? East African medical journal. 1996;73(3):187-90. Epub 1996/03/01. PubMed PMID: 8698019.

20. Sasco AJ, Lowenfels AB, Pasker-de Jong P. Review article: epidemiology of male breast cancer. A meta-analysis of published case-control studies and discussion of selected aetiological factors. International journal of cancer. 1993;53(4):538-49. Epub 1993/02/20. PubMed PMID: 8436428.

21. Korde LA, Zujewski JA, Kamin L, Giordano S, Domchek S, Anderson WF, et al. Multidisciplinary meeting on male breast cancer: summary and research recommendations. Journal of clinical oncology : official journal of the American Society of Clinical Oncology. 2010;28(12):2114-22. Epub 2010/03/24. doi: 10.1200/jco.2009.25.5729. PubMed PMID: 20308661; PubMed Central PMCID: PMCPmc2860409.

22. Bernstein L, Lacey JV, Jr. Receptors, associations, and risk factor differences by breast cancer subtypes: positive or negative? Journal of the National Cancer Institute. 2011;103(6):451-3. Epub 2011/02/25. doi: 10.1093/jnci/djr046. PubMed PMID: 21346225.

23. Yang XR, Chang-Claude J, Goode EL, Couch FJ, Nevanlinna H, Milne RL, et al. Associations of breast cancer risk factors with tumor subtypes: a pooled analysis from the Breast Cancer Association Consortium studies. Journal of the National Cancer Institute. 2011;103(3):250-63. Epub 2010/12/31.

doi: 10.1093/jnci/djq526. PubMed PMID: 21191117; PubMed Central PMCID: PMCPmc3107570.

24. Abreu MH, Afonso N, Abreu PH, Menezes F, Lopes P, Henrique R, et al. Male breast cancer: Looking for better prognostic subgroups. Breast (Edinburgh, Scotland). 2016;26:18-24. Epub 2016/03/29. doi: 10.1016/j.breast. 2015.12.001. PubMed PMID: 27017238.

25. Piscuoglio S, Ng CK, Murray MP, Guerini-Rocco E, Martelotto LG, Geyer FC, et al. The Genomic Landscape of Male Breast Cancers. Clinical cancer research : an official journal of the American Association for Cancer Research. 2016. Epub 2016/03/11. doi: 10.1158/1078-0432.ccr-15-2840. PubMed PMID: 26960396.

Table 1: Distribution of breast cancer tumor characteristics by gender and race

	Both races					Males					Females				
	Males		Females			NHW		NHB			NHW		NHB		
	N	%	N	%	P-value	N	%	N	%	P-Value	N	%	N	%	P-Value
Behavior															
In situ	839	10	190085	16	<0.05	712	10	127	11	>0.05	168728	16	21357	17	<0.05
Invasive	7416	90	977754	84		6396	90	1020	89		872437	84	105317	83	
Grade															
Well differentiated	838	10	168899	14		722	10	116	10		156001	15	12898	10	
Moderately differentiated	3117	38	357081	30	<0.05	2702	38	415	36	>0.05	322181	31	34900	28	<0.05
Poorly differentiated	2140	26	296301	25		1814	26	326	28		250981	24	45320	36	
Undifferentiated	148	2	31225	3		130	2	18	2		28242	3	2983	2	
Unknown	2012	24	314333	27		1740	24	272	24		283760	27	30573	24	
Stage															
In situ	839	10	190083	16		712	10	127	11		168726	16	21357	17	
Localized	3430	42	591008	51	<0.05	3015	42	415	36	<0.05	536754	52	54254	43	<0.05
Regional	3131	38	294022	25		2692	39	439	38		257019	25	37003	29	
Distant	595	7	62245	5		464	7	131	11		51846	5	10399	8	
Unknown	260	3	30481	3		225	3	35	3		26820	3	3661	3	
ER status*															
Negative	287	5	155385	20		226	5	61	8		126995	19	28390	32	
Positive	5109	95	614722	80	<0.05	4396	95	713	92	<0.05	554737	81	59985	68	<0.05
Borderline	7	0	2620	0		6	0	1	0		2283	0	337	0	
PR status*															
Negative	790	15	238139	31		628	14	162	21		200663	30	37476	43	
Positive	4480	84	514348	68	<0.05	3887	86	593	78	<0.05	465447	69	48901	56	<0.05
Borderline	31	1	5277	1		27	1	4	1		4694	1	583	1	
ERPR status**															
ER-PR-	221	5	140583	22	<0.05	173	4	48	8	<0.05	114516	20	26067	36	
ER+PR+	4423	95	501053	78		3843	96	580	92		454240	80	46813	64	<0.05
Her2 status***															
Negative	1061	85	115803	83		890	86	171	84		100856	84	14947	80	
Positive	139	11	19607	14	<0.05	111	11	28	14	>0.05	16507	14	3100	17	
Borderline	42	3	3694	3		37	4	5	2		3099	3	595	3	<0.05
Subtypes****															
Luminal A	1035	87	99444	74		869	87	166	84		88372	76	11072	62	
Luminal B	129	11	13648	10	<0.05	102	10	27	14	>0.05	11591	10	2057	11	<0.05

Her2 Enriched	10	0	5865	4	9	1	1	1	4839	4	1026	6		
Triple Negative	22	2	16006	12	18	2	4	2	12184	10	3822	21		

* These data are restricted to the period 1990-2012 and to patients with a known ER and or PR status. These patients represent at least 65% of the overall sample size.

** These data are restricted to the period 1990-2012.

***These data are restricted to the period 2010-2012 and to patients with known HER2 status. These patients represent at 12 to 15% of the overall sample size.

**** These data are restricted to the period 2010-2012

Table 2: Distribution of hormone and Human Epidermal Growth Factor receptors by age group, gender and race/ethnicity

Age group		Males					Females				
		NHW		NHB			NHW		NHB		
		N	%	N	%	P-value	N	%	N	%	P-value
<50	**ER**										
	Negative	30	7	9	8	>0.05	33271	25	10099	39	<0.05
	Positive	378	93	99	92		102474	75	15554	61	
	PR										
	Negative	78	20	27	27	>0.05	40651	31	11812	47	<0.05
	Positive	320	80	74	73		92495	69	13390	53	
	ERPR										
	Negative	24	7	9	11	>0.05	29261	25	9139	42	<0.05
	Positive	316	93	74	89		88701	75	12509	58	
≥50	**ER**										
	Negative	196	5	52	8	<0.05	93724	17	18291	29	<0.05
	Positive	4018	95	614	92		452263	83	44431	71	
	PR										
	Negative	550	13	135	21	<0.05	160012	30	25664	42	<0.05
	Positive	3567	87	519	79		372952	70	35511	58	
	ERPR										
	Negative	149	4	39	7	<0.05	85255	19	16928	33	<0.05
	Positive	3527	96	506	93		365539	91	34304	67	

Supplemental Material

Table S.1: Distribution survival status by ethnicity, gender and hormone receptor status

		Non-Hispanic White						Non-Hispanic Black					
Estrogen Receptor		Positive			Negative			Positive			Negative		
	Months	Survival (%)	Lower CI	Upper CI	Survival (%)	Lower CI	Upper CI	Survival (%)	Lower CI	Upper CI	Survival (%)	Lower CI	Upper CI
	12	***94.6***	93.7	95.3	***81.6***	75	86.6	***92.8***	90.1	94.9	***75.5***	60.1	85.6
	24	***89.7***	88.5	90.7	***74.2***	66.9	80.1	***83.2***	79.3	86.4	***66.2***	50.3	78.1
Male	36	***84***	82.5	85.3	***70.1***	62.5	76.5	***77.6***	73.1	81.3	***56.2***	40.1	69.5
	48	***77.7***	76	79.3	***65.9***	58	72.7	***69.1***	64.1	73.6	***56.2***	40.1	69.5
	60	***71.9***	70	73.7	***62.6***	54.5	69.7	***62.9***	57.5	67.8	***56.2***	40.1	69.5
	12	***97.4***	97.3	97.4	***94.1***	93.9	94.3	***95.8***	95.6	96	***91.4***	91	91.8
	24	***94.5***	94.4	94.6	***87***	86.7	87.2	***90.9***	90.6	91.2	***81.4***	80.8	81.9
Female	36	***91.2***	91.1	91.3	***81.3***	81	81.5	***86***	85.6	86.4	***74.1***	73.5	74.7
	48	***87.9***	87.8	88	***76.8***	76.5	77	***81.4***	80.9	81.8	***68.7***	68	69.4
	60	***84.6***	84.4	84.7	***73.3***	73	73.6	***77***	76.5	77.5	***64.9***	64.2	65.6
Progesterone Receptor													
	12	***94.8***	93.9	95.6	***88.2***	84.8	90.8	***92.4***	89.2	94.7	***86.8***	79.3	91.7
	24	***90***	88.7	91.1	***81.6***	77.7	84.9	***82.6***	78.1	86.3	***77***	68.3	83.7
Male	36	***84.5***	82.9	85.9	***75.4***	71	79.2	***77.6***	72.6	81.8	***68.1***	58.5	75.9
	48	***77.9***	76.1	79.6	***70.9***	66.3	75	***70***	64.3	74.9	***59.8***	49.8	68.4
	60	***72.1***	70	74	***65.6***	60.7	70	***62.7***	56.6	68.3	***56.4***	46.3	65.3
	12	***97.6***	97.5	97.6	***94.9***	94.8	95	***96.1***	95.9	96.3	***92.1***	91.7	92.4
	24	***94.9***	94.8	95	***88.8***	88.6	89	***91.4***	91.1	91.7	***82.9***	82.5	83.4
Female	36	***91.8***	91.7	91.9	***83.4***	83.2	83.6	***86.8***	86.4	87.2	***75.8***	75.3	76.4
	48	***88.7***	88.5	88.8	***79***	78.8	79.2	***82.3***	81.8	82.8	***70.3***	69.8	70.9
	60	***85.5***	85.4	85.6	***75.3***	75	75.5	***78.1***	77.6	78.6	***66.2***	65.6	66.8

Kaplan-Meier method generated from SEER stat. Confidence interval (CI): Log(-Log()) Transformation. The level is 95%.

