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Master of Public Health

Global Epidemiology

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An abstract of

A thesis submitted to the faculty of the
Rollins School of Public Health of Emory University

in partial fulfillment of the requirements for the degree of
Master of Public Health
in Global Epidemiology

2021

Abstract

This study was planned with the goal to evaluate the potential contribution of racial disparities in obesity to that in breast cancer specific mortality. Previous studies have found that breast cancer risk is associated with non-modifiable factors such as advancing age (65 years and above), genetic factors (BRCA1,2 etc.), early menarche and family history of breast cancer. Modifiable factors highlighted as increasing risk include alcohol consumption, diet, use of post-menopausal hormone replacement therapy and adiposity/obesity. Non-Hispanic Black women experience consistently worse outcomes and higher recurrence and mortality rates which has been attributed to socio economic status, access to care, genetic and pathologic factors that tend to vary with race. This study aimed to examine this phenomenon at a population level with a focus on obesity and breast cancer specific mortality using an ecologic approach with the US census as a framework (states and Census regions, divisions). SEER-STAT and the CDC BRFSS survey results were tapped as sources for our outcome and exposure data respectively. The Joinpoint Regression Analysis program version 4.9 (National Cancer Institute, 2020) was used to examine trends in overall age-adjusted obesity and mortality rates for the 17 states in the southern US region from 1990-2016. Results: The largest gaps between the races in Obesity Average annual percentage change (AAPC) were in Arkansas (NHW AAPC 4%, NHB 1.9%) and Georgia (NHW AAPC %, NHB -3.2%) with the Non-Hispanic Black women experiencing a slower decline in rates than and Non-Hispanic White women. Non-Hispanic White women experienced a more rapid decline in breast cancer mortality in all states; with the widest gaps in Georgia (NHW AAPC -8.0 %, NHB AAPC -3.2%), Oklahoma (NHW AAPC -6.4 %, -0.5%) and Maryland (NHW AAPC -11.2 %, NHB AAPC -6.7%). Similar findings in many states supported an inference that populations with wide racial disparities in obesity also tended to experience five to ten years later, a wide gap in the pattern of breast cancer mortality with the average annual percentage changes being similarly concurrent.

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CHAPTER I: Background

Breast cancer is the most commonly diagnosed cancer worldwide, accounting for nearly 12% of all cases (Kolak et al., 2017). In 2019, Breast cancer was the leading cause of cancer-related death among women with 17.4 million disability-adjusted life years lost, the majority contributed by high middle socio demographic index (SDI) countries including the United States (Global disease burden Collaboration, 2019). It is assumed that one in eight women worldwide will develop mammary gland cancer, only 5-10% of which are caused by genetic factors. The remaining 90-95% are connected to several, often modifiable lifestyle factors (Breast cancer statistics WCRF, 2021).

This warrants a multidisciplinary approach to better understand modifiable factors at various levels – individual, community, and population to enhance knowledge of factors leading to disease occurrence. Obesity/Adiposity, alcohol consumption, reproductive history and post-menopausal hormone replacement are among the major causative factors discovered (Kolak et al., 2017). Primary prevention of breast cancer through lifestyle modification may be an effective strategy to mitigate the increasing morbidity, mortality and economic costs incurred due to breast cancer. Obesity's potential contribution to breast cancer mortality is a major concern since the United states saw the world's largest absolute increase in the number of obese people between 1980 and 2008 - 56 million (Stevens et al., 2012).

Health equity is an emerging public health goal in the United States with the recognition of persistent disparities in health outcomes among minority racial and ethnic communities. To reduce inequity, governments and health care organizations may consider what contributes to the disparities such as unique risk factors among minority groups, and disproportionate lack of access to diagnosis and treatment. In addition, a commitment to collecting meaningful data to understand local needs and priorities and ongoing assessment of health outcomes are vital to maintaining progress (Wong, LaVeist, & Sharfstein, 2015).

Non-Hispanic Black women have been documented to have up to twice higher breast cancer specific mortality risk compared to non-Hispanic White women (Akinyemiju, Moore, Ojesina, Waterbor, & Altekruse, 2016). In 2018, Non-Hispanic Black adults had the highest age-standardized prevalence of obesity (49.6%) while the rate among non-Hispanic White adults was 42.2% (Hales, Carroll, Fryar, & Ogden, 2020). While the relationship between obesity and cancer incidence is well documented, there remains a need to better explore its contribution to breast cancer-specific mortality and the racial disparities therein. A community-wise or geographic perspective would help fill this need by localizing the disparities and inform resource allocation for preventive interventions.

Breast cancer – Risk factors and Epidemiology

Breast cancer is the most diagnosed cancer among women in the US with 268,600 new cases in 2019. Having caused 41760 deaths in the same year, it remains the second leading cause of cancer mortality – exceeded only by lung and bronchus cancers (DeSantis et al., 2019).

Among the major non-modifiable risk factors for breast cancer are certain inherited genetic mutations (such as BRCA1, BRCA2) (Bogdanova, Helbig, & Dörk, 2013), Female biological sex and advancing age (peaks around 60 years) (Sun et al., 2017). Family and personal history of breast cancer, early radiation exposure, mammographically dense breasts, early menarche and late menopause constitute a few other risk factors that are outside of an individual's control (Majeed et al., 2014).

This brings us to risk factors that are modifiable, namely alcohol consumption, oral contraceptive use, menopausal hormone replacement therapy and obesity (Sun et al., 2017). Physical exercise/ weight control (Bianchini, Kaaks, & Vainio, 2002), and earlier pregnancy and breastfeeding for at least one year (Sun et al., 2017) have been documented as protective.

1.2 Role of Obesity

Recent decades have seen an unprecedented rise in obesity with 600 million people worldwide considered obese - defined in terms of a body mass index greater than 30 kg/m^2. In the United states, 42% of adults and 43% of women fulfilled the criteria in 2018 (Hales et al., 2020). It is a comorbidity that exists alongside several disease conditions including cancers and affects their outcomes.

A 1.3- to 1.5-fold increase in breast cancer risk was shown in postmenopausal women with obesity. This increase exhibited a 'dose-response' effect with a 1.09- to 1.31- fold increase for every 5 kg/m^2 rise in BMI, especially among those who never used hormone replacement therapy (Renehan, Zwahlen, & Egger, 2015) . Moreover, obesity appeared to increase this risk even in geographical areas with historically low and moderate risk, thus warning of a possible rapid rise of risk with obesity. In women diagnosed with breast cancer, obesity has been associated with greater risk for the occurrence of cancers at other sites, contralateral breast cancers and all-cause mortality (Dignam et al., 2006). Obese breast cancer patients are at increased risk for morbidities during their clinical course and recovery including surgical wound complications, lymphoedema and possibly, congestive heart failure if treated with doxorubicin (McTiernan, 2018).

There are multiple mechanisms studied by which obesity increases cancer risk. Endocrine factors secreted by adipose tissue that have been studied in this regard are IGF-1 (*insulin-like growth factor*), estrogens, leptin or adiponectin (Laurent, Nieto, Valet, & Muller, 2014). Mammary adipose tissue also releases cytokines that promote inflammation such as interleukin 6 or TNFα (tumor necrosis factor alpha). A complication of obesity, hyperinsulinemia has also been implicated (Laurent et al., 2014).

Obese patients and those with diabetes frequently have elevated levels of cholesterols such as very-low-density lipoprotein (VLDL), triglycerides, low-density lipoprotein (LDL), and high-density lipoprotein (HDL) (Chahil & Ginsberg, 2006). Elevated total cholesterol and triglycerides coupled with decreased HDL cholesterol have been associated with an 18%, 15%, and 20% increased risk of cancer, respectively (Melvin et al 2013). Breast cancers in obese postmenopausal women also tend to express estrogen and progesterone receptors, which both impact prognosis (Renehan et al., 2015).

Racial disparities in breast cancer outcomes

Non-Hispanic Black women have had up to twice as high breast cancer specific mortality risk compared to non-Hispanic White women (Akinyemiju et al., 2016). Later stage at diagnosis, differences in tumor characteristics (estrogen receptor negative) and in prevalence of comorbidities have been said to explain a part of the disparity (Jemal et al., 2018). Insurance and socioeconomic factors that influence access to timely diagnostic services and healthcare are also major contributing factors to the gap. Black women are also less likely to live in areas with good healthcare access and are less likely to receive surgical treatment for breast cancer compared to their White counterparts (Akinyemiju et al., 2016).

Existing studies of ecological design

In two novel studies in 2012 and 2014 examining city-level data for racial disparities in breast cancer mortality in the United States, Non-Hispanic Black to non-Hispanic White mortality rate ratios were calculated as the main measures of disparity. Mortality in Black women compared to White women was found to be significantly greater than the null in many of the cities studied (Whitman, Orsi, & Hurlbert, 2012). The ecological design of these studies allowed examination of large numbers of individuals over an extended period of time (20 years) and lent a vital geographic dimension to the results (Hunt, Silva, Lock, & Hurlbert, 2019). It also enabled the investigators to study several variables at the ecological level as potential correlates. The increase in the disparity was apparent as White mortality rates improved substantially over the 20-year study period, while rates in the Black population did not improve by a significant amount. The authors agreed that the use of this type of design is vital to progress towards mitigating the wide racial disparities.

CHAPTER II

Title: Potential contribution of obesity to disparate breast cancer outcomes: an ecologic study

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Abstract:

This study was planned with the goal to evaluate the potential contribution of racial disparities in obesity to that in breast cancer specific mortality. Previous studies have found that breast cancer risk is associated with non-modifiable factors such as advancing age (65 years and above), genetic factors (BRCA1,2 etc.), early menarche and family history of breast cancer. Non-modifiable factors highlighted as increasing risk include alcohol consumption, diet, use of post-menopausal hormone replacement therapy and adiposity/obesity. Non-Hispanic Black women experience consistently worse outcomes and higher recurrence and mortality rates which has been attributed to socio economic status, access to care, genetic and pathologic factors that tend to vary with race. This study aimed to examine this phenomenon at a population level with a focus on obesity and breast cancer specific mortality using an ecologic approach with the US census as a framework (states and Census regions, divisions). SEER-STAT and the CDC BRFSS survey results were tapped as sources for our outcome and exposure data respectively. The Joinpoint Regression Analysis program version 4.9 (National Cancer Institute, 2020) was used to examine trends in overall age-adjusted obesity and mortality rates for the 17 states in the southern US region from 1990-2016. Results: The largest gaps between the races in Obesity Average annual percentage change (AAPC) were in Arkansas (NHW AAPC 4%, NHB 1.9%) and Georgia (NHW AAPC %, NHB -3.2%) with the Non-Hispanic Black women experiencing a slower decline in rates than and Non-Hispanic White women. Non-Hispanic White women experienced a more rapid decline in breast cancer mortality in all states; with the widest gaps in Georgia (NHW AAPC -8.0 %, NHB AAPC -3.2%), Oklahoma (NHW AAPC -6.4 %, -0.5%) and Maryland (NHW AAPC -11.2 %, NHB AAPC -6.7%). Similar findings in many states supported an inference that populations with wide racial disparities in obesity also tended to experience five to ten years later, a wide gap in the pattern of breast cancer mortality with the average annual percentage changes being similarly concurrent.

Introduction

Breast cancer is the second leading cause of cancer mortality among women (Global disease burden Collaboration, 2019) and is responsible for substantial morbidity and mortality in the US population. While the past few decades have seen an improvement in breast cancer mortality in the general population, Black women remain disproportionately affected with mortality rates that have not seen the same decline as their White counterparts (Akinyemiju et al., 2016). Among the major modifiable risk factors of breast cancer recurrence and mortality is obesity/adiposity – an ever-rising phenomenon in the United States. Obesity has been associated with an increased risk of incidence, recurrence, worse prognosis and mortality in breast cancer (Renehan et al., 2015).

This study was planned with an overall goal to evaluate the potential contribution of obesity to the disparity in breast cancer mortality between non-Hispanic White and non-Hispanic Black women in the United States. An ecologic approach to the study design was chosen to facilitate the detection of population-level trends i.e., state and census region. Trend analysis is an emerging group of methods for the study of population level health outcomes. Join point regression is a trend analysis protocol that selects the best fitting piecewise continuous log-linear model for a given line. The permutation test is then conducted to determine the minimum number of "join points" necessary to fit the data. Especially suited to the analysis of time-based trends, annual percentage change and average annual percentages changes are generated to describe the trajectory and inform predictions. The application of these methods in population cancer research was first demonstrated in a 2000 paper describing trends of the most common types of cancer in the United States (Kim, Fay, Feuer, & Midthune, 2000).

Since 10 years is regarded as the "average" lag period for obesity related cancer development risk (De Pergola & Silvestris, 2013), trends in breast cancer mortality data were examined with a 5- and 10-year lag to the corresponding obesity trend lines. The specific aims of this study were:

(i) To describe US state-wise prevalence of obesity among Non-Hispanic White and Non-Hispanic Black women over a 25-year period (1990-2015) and characterize the disparities between the two groups.

(ii) To describe US state-wise rates for breast cancer specific mortality over a 25-year period (1990-2015) and characterize the disparities between the two groups.

(iii) To detect 'spikes' in trends of obesity and breast cancer specific mortality using Join point regression. Then, systematically compare the trends and highlight any apparent concurrence in patterns of breast cancer mortality with a 5- and 10-year lag to the corresponding obesity trends at state and regional levels.

Methods

Study design and population

This study utilized an ecological design with data obtained at the state level. Exposure data comprised state-level self-reported obesity prevalence data *(*BRFSS). Race/ and ethnicity data were also collected alongside obesity prevalence data. The primary outcome was breast cancer mortality according to state and race/ethnicity as well as year it was sourced from the Surveillance, Epidemiology, and End Results (SEER) Program of the National

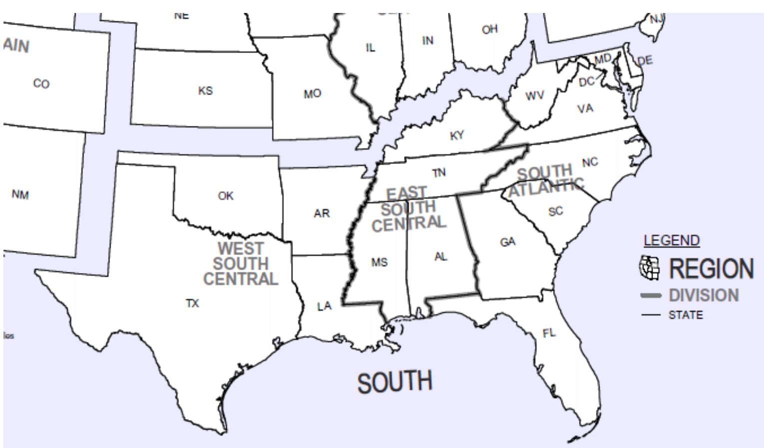


Figure 1 US Census regions

Cancer Institute. This study was restricted to women with mortality specifically attributed to breast cancer. Mortality case counts of less than 10 in any state or year were excluded.

Following initial descriptive analyses, the population of interest was restricted to the Southeastern census region of the USA (17 states, Fig 1) since these states have higher proportions of non-Hispanic Black populations (*Office of minority health USA Census* 2019), which would allow for better estimates of racial disparities in breast cancer mortality rates.

Region 3: South		
Division 5: South Atlantic	**Division 6: East South Central**	**Division 7: West South Central**
Delaware (10)	Alabama (01)	Arkansas (05)
District of Columbia (11)	Kentucky (21)	Louisiana (22)
Florida (12)	Mississippi (28)	Oklahoma (40)
Georgia (13)	Tennessee (47)	Texas (48)
Maryland (24)		
North Carolina (37)		
South Carolina (45)		
Virginia (51)		
West Virginia (54)		

Figure 2 US Census Southern region divisions

Trend comparisons for obesity and breast cancer mortality have been done at the state, regional division and overall region levels as defined by the map in Figure 1. Regional divisions were used as geographic units of inquiry as a middle-order step between the state and regional levels to facilitate possible location-based insights into the prevalence and influence of obesity on cancer mortality. The divisions were defined as in Figure 2.

Exposure Data

The Behavioral Risk Factor Surveillance System (BRFSS) is a nation-wide health-related telephone survey conducted and compiled annually since 1984 by the Centers for Disease control. Data collected include health related behaviors, chronic health conditions and use of preventive measures and services, organized into a complex stratified database. This study utilized self-reported body weight and height data from the BRFSS 1990 to 2016. Body Mass Index, defined as the weight in kilograms divided by the square of the height in meters, was calculated using self-reported height and weight data as a proxy for obesity prevalence (Table 1).

Outcome Data

Breast cancer mortality categorized by state, race/ethnicity and year sourced from the Surveillance, Epidemiology, and End Results (SEER) Program database of the National Cancer Institute. The mortality rates were age-standardized to the population of the United States in 2000.

The “time lag” in cancer development in the presence of adiposity due to obesity implies that the typical follow up period is longer than 10 years in most cohorts assessing cancer risk (De Pergola & Silvestris, 2013). Thus, 10 years is regarded as the “average” lag period for obesity related cancer development. We examined for changes in race-specific mortality trends with a 5- and 10-year lag to the corresponding obesity trend line. A decision was made to calculate 2-year averages of mortality rates at 5-year increments to stabilize rates and reduce noise in the trend lines from 1990 to 2016.

Data extraction and calculation

Annual breast cancer specific mortality data for pairs of years in 5-year increments from 1990 to 2016 was extracted from the SEER database using the SEER*Stat interface. Two-year averages were first calculated (1990-91, 1995-96 etc. up to 2015-16) following which mortality rate differences between Non-Hispanic Black and Non-Hispanic White populations were obtained (table 2).

Obesity data categorized by race and year were extracted using SAS-callable SUDAAN. The data sets were first sorted by survey strata and primary sampling unit serial numbers and variable names suitably standardized using the BRFSS codebook. The cut-off used for obesity was a body mass index of 30.00 or greater (Apovian, 2016). The datasets were then concatenated, and the survey weight variable was divided by the total number of datasets i.e. 12. 'Proc cross tab' was then used to obtain state-wise tables of obesity rates categorised by race and 'Proc R logist' function was used to obtain adjusted rates. Exposure and outcome data for each state contained a timeline of 26 years (1990-2016) comprising 6 data points, each denoting a 2-year average rate for obesity or breast cancer mortality. The data were further cleaned and formatted suitably to be imported into the analysis software.

Validation of breast cancer mortality data

The mortality data were compared to data from corresponding periods compiled by American Cancer Society sourced from the biannual 'breast cancer – facts and figures' documents published on their website (Table 3). ACS breast cancer mortality data are publicly available starting from 1998 in 4-year periods up to 2015. The mortality rates for both race categories are lower in the ACS data compared to SEER data. However, the rates for each state and both races are similarly downward trending overall. Mortality rate differences in the South Atlantic region were the lowest overall throughout the study period.

Trend visualization and descriptive analysis

The exposure and outcome datasets were exported to Excel™ where the obesity prevalence differences between Non- Hispanic Black and Non-Hispanic White populations were calculated. The tables were suitably modified using macros and pivot table functions to obtain formats suitable for trend visualization. The graphs comprised the study period in 5-year increments on the x-axis and mortality or obesity rates on the y-axis. The trend figures for each state, census sub-division, and the overall southern region of the US each contain a line for Non- Hispanic Black, Non-Hispanic White and the rate difference or prevalence difference.

Obesity rates for non-Hispanic Black populations were higher in a large majority of state and region trends. prevalence difference in obesity and mortality rate difference were the measures chosen to highlight disparities among the race categories. (Table 1, 2). Trends were examined using the US census scheme for the Southern United States with South Atlantic, East south central and West south-central divisions as shown in Figures 2.

In the overall trend for the southern US (Figure 3), Obesity rates remain consistently higher among non-Hispanic Black population with the prevalence difference peaking in 2005-2006. The mortality rates on the other hand are close together with a crossover of trend line in 1995-1996. The widest gap i.e., highest rate difference between NHW and NHB occurs in 2010-2011 – 5 years after the peak in obesity prevalence difference.

South Atlantic division (comprising DE, DC, FL, GA, MD, NC, SC, VA, WV) (Fig 4)

Obesity prevalence differences between non-Hispanic White and non-Hispanic Black populations widened around 2005-2006 and apparently plateaued for the following decade. The mortality rate difference shows a late gradual uptick in the decade following the rise in obesity prevalence difference. Similar to the ACS data, mortality differences between NHB and NHW were the lowest in the South Atlantic sub-division compared to all the others.

Examining a few states in particular, the obesity trend line for both Non-Hispanic Black and Non – Hispanic White women in Georgia (Fig 4a) show substantial peaks in 2000-2001 and are followed by a marked uptick in breast cancer mortality rate in 2005-2006 for NHB and 2010-2011 for NHW. Obesity prevalence difference spikes in 2000-2001 and in 2010-2011. These are followed by rises in mortality rate differences in 2005-2005 and 2015-2016. Maryland (Fig 4b) saw a rise in obesity prevalence among NHB population in 2005-2006, which also increased the prevalence difference. This was followed by a spike in NHB mortality rate and thus the rate difference in 2010-11. Obesity prevalence difference in North Carolina (Fig 4c) rises sharply in 1995-1996 and then rises gradually until 2010-2011. Mortality rate difference shows a similar rise peaking in 2005-2006.

East South-Central Division (AL, KY, MS, TN) (Fig 5)

The trend line for obesity prevalence difference spikes in 2000-2001 and is followed by a widening of the gap in mortality rate in 2005-2006 and 2010-2011. Alabama (Fig 5a) shows a widening of the gap in obesity prevalence in 1995-1996 and 2005-2006 and followed by gradual and constant rise in mortality prevalence difference in 2005-2006. In Mississippi (Fig 5c), obesity prevalence difference line peaks in 2000-2001 while the gap in mortality rate difference is highest in the following 5 years, i.e., 2005-2006. Tennessee (Fig 5d) saw a rise is obesity prevalence difference starting from 1995-1996 and ending in a spike in 2005-2006. This precedes a spike in mortality rate difference in 2005-2006 with a similarly wide gap in 2010-2011.

West South-Central division (AR LA OK TX) (Fig 6)

Obesity spikes in 2000-2001 with an overall rise until 2015. This coincides with a consistent widening of the mortality rate difference from 2000-2001 up to 2015. Louisiana (Fig 6a) shows a 2005-2006 peak in obesity prevalence difference which precedes a marked widening between the mortality trend lines with a peak in mortality rate difference in 2010-2011. In Texas (Fig 6b), a 1995-1996 peak in obesity prevalence difference is followed by a mortality rate difference peak in 2010-2011.

Trend Analysis: Joinpoint Regression

The Joinpoint Regression Analysis program version 4.9 (National Cancer Institute, 2020) was used to examine trends in overall age-adjusted mortality rates for the 17 states in the southern US region from 1990-2016. The Joinpoint program selects the best fitting piecewise continuous log-linear model. The permutation test was performed to determine the minimum number of "joinpoints" necessary to fit the data (Kim et al., 2000). A significance level of 0.05 was used for the permutation test. The program estimated and displayed graphically the state-wise annual percent change (APC) with 95% confidence intervals for the 26-year study period. Average annual percentage change was reported with a 95% confidence interval to construct a more complete picture over the study period.

Results

The joinpoint regression with permutation test at 95% confidence interval was performed for both exposure and outcome variables, categorized by state and race (Table 4, 5).

A positive annual average percentage change implies a generally upward trend while a negative AAPC describes a downward one. Across all states and race categories, obesity saw an upward trend with most states having a statistically significant confidence interval i.e., that the increase in obesity prevalence was sufficiently different from zero across two-and-a-half-decade the study period. Breast cancer specific mortality on the other hand showed a negative AAPC signifying downward trends across all states and race categories.

Non-Hispanic White women in Georgia (AAPC 4.3%, 95 % CI 0.9, 7.7), Mississippi (3.9% 95 % CI 1.8 , 6.1), Oklahoma (3.8%, 95 % CI 2 , 5.7) and Tennessee (3.7%, 95 % CI 0.7 , 6.8) experienced the steepest rise in obesity in this study period. For NHB women, the steepest rise in obesity was in Kentucky (AAPC 3.3%, 95% CI 1.3, 5.3), Maryland (2.9%, 95% CI 1.5,4.2), Tennessee (2.6%, 95% CI 0.5, 4.7), and Georgia (2.6%, 95% CI 0,5.4). The largest gaps in obesity AAPC were in Arkansas (NHW AAPC 4%, NHB AAPC -0.4,4.2) and Georgia with the NHB women experiencing a slower decline in rates than and Non-Hispanic White women. Kentucky on the other hand had the smallest gap of just 0.1% (NHW AAPC 3.3%, NHB AAPC 3.2%) i.e., the rates remained almost stationary throughout the study period.

With our outcome of interest, i.e., breast cancer specific mortality, White women across the board tended to have a steeper decline (i.e., improvement) in mortality rates. The one exception was Kentucky where Black women had steeper fall in breast cancer mortality [NHB -9.4% (-14.8,-3.7), NHW -7.3% (-8.5,-6)]. Non-Hispanic White women experienced a more rapid decline in breast cancer mortality in all states with the widest gaps in Georgia [NHW AAPC -8.0 % (-

9.8,-6.1), NHB -3.2% (-7.1,0.9)], Oklahoma [NHW AAPC -6.4 % (-7.7,-5) , NHB AAPC -0.5 (-8.8, 8.5)] and Maryland [NHW AAPC -11.2 % (-13.3, -9), NHB AAPC -6.7% (-10.3,-2.9)].

Discussion

While the results of our join point regression analyses make apparent the marked difference in the way Non-Hispanic White and Black women experienced acceleration or decline in obesity and breast cancer mortality, a concurrent examination of the visual trend lines gives us a more comprehensive picture of the population level dynamics of these health parameters.

Georgia showed the widest disparities in obesity rates (NHB consistently higher than NHW with a large rate difference) coupled with the widest gaps in breast cancer mortality rates (NHW rates falling more rapidly than NHB) with an apparent 5- and 10- year lag time from the spikes in obesity rate difference (2000-2001, 2010-2011) to those in mortality rates (2005-2006, 2015-2016). Maryland showed a similar 5-year concurrence of obesity rated difference to mortality rate difference with a steep rise in NHB obesity and one of the widest gaps in BC mortality AAPC (NHW women had a much faster improvement in mortality compared to NHB women).

Tennessee, Mississippi, and Texas had similar findings supporting an inference that populations with wide racial disparities in obesity also tended to experience five to ten years later, a wide gap in the pattern of breast cancer mortality with the average annual percentage changes being concurrent.

These insights will aid identification of communities in need and can support advocacy for changes in medical guidelines to include weight management as a recurrence risk reducer for breast cancer survivors. These results may also be used to inform allocation of resources for targeted risk-reducing interventions. Further, as the United States looks to address inequities in health at a national level, knowledge of which populations experience increased mortality will help promote tailor-made programs that are culturally sensitive and thus attract community buy-in.

The ecologic design of our study precludes individual level correlation and cannot be used to infer a cause-and-effect relationship between the exposure and outcome data. However, this design does allow an initial examination of the health status and needs of communities, which was the intended goal. A prospective cohort design would be the ideal format to definitively explore individual level risk for breast cancer mortality in women with obesity across race categories.

TABLES

Table 1: 2-year Avg Obesity Prevalence (%) for Non-Hispanic White (NHW), and Non-Hispanic Black (NHB) and Prevalence difference (PD), 1990-2016

State/Sub-division	Race Category/ Prevalence difference (PD)	1990-1991	1995-1996	2000-2001	2005-2006	2010-2011	2014-2015
Alabama	NHW	10.74	15.33	21.37	24.47	28.82	28.65
	NHB	23.73	33.67	38.75	45.62	46.41	48.91
	PD	12.99	18.34	17.38	21.15	17.59	20.26
Arkansas	NHW	11.83	15.72	19.73	25.33	37.13	33.56
	NHB	37.42	27.05	40.2	47.78	42.79	49.21
	PD	25.59	11.33	20.47	22.45	5.66	15.65
Delaware	NHW	13.02	16.52	17.01	21.20	24.68	29.30
	NHB	32.76	31.69	32.49	39.64	41.9	49.33
	PD	19.74	15.17	15.48	18.44	17.22	20.03
Washington DC	NHW	4.66	5.75	7.55	7.58	6.88	10.61
	NHB	27.35	27.49	35.95	38.61	41.89	43.03
	PD	22.69	21.74	28.40	31.03	35.01	32.42
Florida	NHW	10.81	14.22	16.12	18.64	22.18	22.67
	NHB	25.47	29.98	35.06	40.17	38	37.44
	PD	14.66	15.76	18.94	21.53	15.82	14.77
Georgia	NHW	8.32	9.48	18.41	22.22	24.25	26.48
	NHB	21.02	20.6	35.58	38.46	45.71	40.95
	PD	12.70	11.12	17.17	16.24	21.46	14.47
Kentucky	NHW	13.10	17.95	22.12	27.99	27.47	30.10
	NHB	26.82	26.86	35.04	44.36	58.01	50.22

	PD	13.72	8.91	12.92	16.37	30.54	
Louisiana	NHW	12.02	16.05	19.99	22.66	25.91	28.96
	NHB	24.64	28.86	36.65	42.83	44.76	47.18
	PD	12.62	12.81	16.66	20.17	18.85	18.22
Maryland	NHW	9.08	15.47	17.92	19.93	20.76	27.03
	NHB	21.38	29.09	31.54	39.5	42.26	45.09
	PD	12.30	13.62	13.62	19.57	21.50	18.06
Mississippi	NHW	11.22	15.36	19.29	25.56	30.76	28.77
	NHB	30	34.98	42.23	46.32	48.6	50.93
	PD	18.78	19.62	22.94	20.76	17.84	22.16
North Carolina	NHW	11.60	14.09	18.59	23.09	23.97	26.14
	NHB	23.61	34.36	39.85	46.45	48.67	45.16
	PD	12.01	20.27	21.26	23.36	24.70	19.02
Oklahoma	NHW	11.69	14.64	19.56	25.40	32.02	31.07
	NHB	22.99	25.01	31.97	35.15	42.38	40.88
	PD	11.30	10.37	12.41	9.75	10.36	9.81
South Carolina	NHW	10.73	13.43	17.43	23.63	26.63	25.68
	NHB	26.06	30.31	39.57	44.4	51.42	49.74
	PD	15.33	16.88	22.14	20.77	24.79	24.06
Tennessee	NHW	10.02	17.25	20.89	25.58	21.96	26.74
	NHB	26.68	27.35	37.38	46.63	41.22	45.24
	PD	16.66	10.10	16.49	21.05	19.26	18.50
Texas	NHW	9.50	13.83	18.82	23.39	23.93	24.05
	NHB	20.93	33.43	33.23	36.18	42.27	41.84
	PD	11.43	19.60	14.41	12.79	18.34	17.79
Virginia	NHW	9.73	15.76	16.45	22.82	22.82	24.35
	NHB	25.45	28.24	33.32	40.47	45.24	42.62
	PD	15.72	12.48	16.87	17.65	22.42	18.27

West Virginia	NHW	15.26	19.30	23.98	29.82	36.18	34.05
	NHB	27	39.34	29.18	50.21	40.53	44.61
	PD	11.74	20.04	5.20	20.39	4.35	10.56
South Overall	NHW	10.78	14.72	18.54	22.47	25.67	26.95
	NHB	26.08	29.90	35.76	42.52	44.83	45.43
	PD	15.29	15.19	17.22	20.05	19.16	18.48
West South Central	NHW	18.61	24.07	23.72	29.66	30.12	30.10
	NHB	26.495	28.5875	35.5125	40.485	43.05	44.7775
	PD	7.88	4.52	11.79	10.83	12.93	14.67
East South Central	NHW	14.24	20.59	20.47	30.01	28.48	29.67
	NHB	26.8075	30.715	38.35	45.7325	48.56	48.825
	PD	12.57	10.12	17.88	15.72	20.08	19.15
South Atlantic	NHW	17.52	20.37	24.77	29.12	30.83	31.27
	NHB	25.57	30.12	34.73	41.99	43.96	44.22
	PD	8.05	9.75	9.96	12.87	13.13	12.95

Table 2: 2-year Avg Breast Cancer Mortality rate (per 100,000) for Non-Hispanic White (NHW), and Non-Hispanic Black (NHB) and Rate difference (RD) , 1990-2016,

Source: NCI SEER database, standardized to 2000 US population.

State/Sub-division	Race Category/ Rate difference (RD)	1990-1991	1995-1996	2000-2001	2005-2006	2010-2011	2015-2016
Alabama	NHW	39.5	35.5	36.2	31.9	27.8	27.7
	NHB	53.6	49.2	48	47.6	43.9	39.9
	RD	14.10	13.70	11.80	15.70	16.10	12.20
Arkansas	NHW	38.8	35.8	31.6	31.7	28.5	26.9
	NHB	50.4	50.9	48	48.8	46.4	41.5
	RD	11.60	15.10	16.40	17.10	17.90	14.60
Delaware	NHW	52.9	44.3	39.1	32	30.8	29.7
	NHB	56.8	53.3	46.5	29.5	36.5	33.9
	RD	3.90	9.00	7.40	-2.50	5.70	4.20
Washington DC	NHW	48.2	31.6	40.1	31.6	30.4	20.5
	NHB	68.1	68.9	53.7	45.2	46.8	45.9
	RD	19.90	37.30	13.60	13.60	16.40	25.40
Florida	NHW	43.4	39.9	32.5	29.6	28.6	25.5
	NHB	51.8	47.3	42.7	41.7	37	34.5
	RD	8.40	7.40	10.20	12.10	8.40	9.00
Georgia	NHW	41.2	36.5	33.8	29.9	29.6	26.8
	NHB	43.3	49.6	41.9	44.4	40.9	39.4
	RD	2.10	13.10	8.10	14.50	11.30	12.60
Kentucky	NHW	42.4	39.2	37.1	33.4	30.5	29.7
	NHB	54.2	58.2	46.4	37.2	39.1	36.2
	RD	11.80	19.00	9.30	3.80	8.60	6.50
Louisiana	NHW	43	42.4	37.9	34.2	28.8	27

	NHB	59.7	54.2	55.4	54	49.5	40.8
	RD	16.70	11.80	17.50	19.80	20.70	13.80
Maryland	NHW	47.8	44.2	36.7	34.1	28.7	27.6
	NHB	54.5	53.5	47	41.2	44.4	38.3
	RD	6.70	9.30	10.30	7.10	15.70	10.70
Mississippi	NHW	36.8	36.1	35.8	30.5	28.5	27.7
	NHB	51.3	51.8	51.8	50	44	40
	RD	14.50	15.70	16.00	19.50	15.50	12.30
North Carolina	NHW	42	37.3	32.1	31.5	29.7	26.6
	NHB	49.4	55.8	45.7	46.4	41.5	39.2
	RD	7.40	18.50	13.60	14.90	11.80	12.60
Oklahoma	NHW	42.5	41.5	36.9	35.6	33.5	30.6
	NHB	39.9	54.7	55.5	45.6	47.7	46.9
	RD	-2.60	13.20	18.60	10.00	14.20	16.30
South Carolina	NHW	43.7	37.7	33.8	32.6	30	27.6
	NHB	54.1	48.9	50.6	44.1	42.1	37.4
	RD	10.40	11.20	16.80	11.50	12.10	9.80
Tennessee	NHW	41.2	39.2	35.2	33.1	28.5	29.5
	NHB	59.2	53.7	46.9	54.4	47.8	39.6
	RD	18.00	14.50	11.70	21.30	19.30	10.10
Texas	NHW	39.7	38.1	33.9	30.9	27.5	26.9
	NHB	54.3	52.8	51.2	47.7	44.8	39.5
	RD	14.60	14.70	17.30	16.80	17.30	12.60
Virginia	NHW	47.7	39.1	37.2	33.8	29.6	28.8
	NHB	54.6	58.1	55.9	48.5	44	38.6
	RD	6.90	19.00	18.70	14.70	14.40	9.80
West Virginia	NHW	41.5	38.5	37.3	33.5	31.2	29.9
	NHB	47.9	54.8	52.2	46.1	26.2	43.1

	RD	6.40	16.30	14.90	12.60	-5.00	13.20
South Overall	NHW	44.83	40.44	35.84	32.27	29.24	27.69
	NHB	40.44	40.16	37.58	33.70	32.79	29.23
	RD	-4.39	-0.28	1.73	1.43	3.56	1.54
West South Central	NHW	41.00	39.45	35.08	33.10	29.58	27.85
	NHB	51.08	53.15	52.53	49.03	47.10	42.18
	RD	10.08	13.70	17.45	15.93	17.53	14.33
East South Central	NHW	39.98	37.50	36.08	32.23	28.83	28.65
	NHB	54.58	53.23	48.28	47.30	43.70	38.93
	RD	14.60	15.73	12.20	15.08	14.88	10.28
South Atlantic	NHW	45.38	38.79	35.84	32.07	29.84	27.00
	NHB	53.39	54.47	48.47	43.01	39.93	38.92
	RD	8.01	15.68	12.62	10.94	10.09	11.92

Table 3: 2-year Avg Breast Cancer Mortality rate (%) for Non-Hispanic White (NHW), and Non-Hispanic Black (NHB) and Rate difference (RD), 1990-2016,

Source: American Cancer Society, age standardized to 2000 US population**.**

	1998-2002			2000-2004			2002-2006			2003-2007			2006-2010			2008-2012			2011-2015		
State/ Sub Division	NHW	NHB	RD	NHW	NHB	RD	NHW	NHB	RD	NHW	NHB	RD	NHW	NHB	RD	NHW	NHB	RD	NHW	NHB	RD
Alabama	24.8	32.3	7.5	24.5	31.6	7.1	23.2	31.5	8.3	22.7	32.3	9.6	21	31.5	10.5	20.4	30.7	10.3	20	28.5	8.5
Arkansas	22.7	37.4	14.7	22.8	34.9	12.1	22.8	34.9	12.1	23.3	33.4	10.1	22.3	32.9	10.6	21.4	31.4	10	20.5	30.3	9.8
Delaware	26.9	35.8	8.9	25.3	32.7	7.4	23.5	27.9	4.4	24.7	25.4	0.7	23.3	23.4	0.1	21.9	26.5	4.6	21.2	26	4.8
Washington DC	28.8	40.2	11.4	26.7	36.1	9.4	23.1	32.4	9.3	22.9	31.8	8.9	22.6	34.7	12.1	24.1	34	9.9	22.6	34.4	11.8
Florida	23.5	30.8	7.3	22.8	30.5	7.7	21.8	30	8.2	22.1	29.7	7.6	21.5	29.1	7.6	21.3	28.5	7.2	20.1	25.8	5.7
Georgia	24.1	32	7.9	24	30.8	6.8	22.5	30.9	8.4	22.2	30.4	8.2	21.9	29.6	7.7	21.2	29.5	8.3	20.1	29.2	9.1
Kentucky	26.5	36.8	10.3	25.5	36.6	11.1	24.4	33.6	9.2	23.9	33	9.1	22.7	32.9	10.2	22.1	32.7	10.6	21.4	28.5	7.1
Louisiana	26.4	38.6	12.2	25.7	40.3	14.6	24.6	40	15.4	24.2	37.7	13.5	22.7	33.8	11.1	21.9	34.8	12.9	20.2	33.6	13.4
Maryland	26.9	35.1	8.2	25.9	34	8.1	25.2	32.5	7.3	24.7	31.8	7.1	22.8	31.7	8.9	22.1	30.6	8.5	21.2	28.1	6.9
Mississippi	24	36.6	12.6	24.1	36.3	12.2	22.4	35.8	13.4	22.1	34.6	12.5	20.8	33.4	12.6	20.4	33.3	12.9	19.5	31.5	12
North Carolina	23.8	35.1	11.3	23.5	33.4	9.9	#	33.5	10.4	23	33.7	10.7	21.9	29.9	8	21	28.8	7.8	19.7	29.1	9.4
Oklahoma	26.2	39.5	13.3	25.6	37.9	12.3	#	34.4	9.4	25.1	32.7	7.6	24	34.7	10.7	23	35.4	12.4	23	33.6	10.6
South Carolina	24.5	35.2	10.7	23.2	33.4	10.2	#	31.5	8.7	22.2	31.2	9	21.3	29.8	8.5	21.1	29.2	8.1	20.5	29	8.5
Tennessee	25.4	34	8.6	25	35.6	10.6	#	37.3	13.2	23.7	38	14.3	21.8	35.4	13.6	21.2	33.9	12.7	20.7	31.5	10.8
Texas	24.4	36	11.6	23.6	36.2	12.6	#	35.1	12.6	23.3	35.3	12	22	33.5	11.5	21.1	33.7	12.6	20.6	30.4	9.8
Virginia	26	37.4	11.4	25.4	37.1	11.7	#	35.1	10.7	24.3	34.7	10.4	22.8	33.2	10.4	21.6	31.7	10.1	21	29.5	8.5
West Virginia	25.9	38.5	12.6	25.2	36.2	11	#	33.9	9.7	24.2	33.9	9.7	22.2	25.8	3.6	22.7	26.6	3.9	22.2	30.5	8.3
South Overall		35.96	10.62	24.64	34.92	10.28	23.51	33.55	10.04	23.45	32.92	9.47	22.21	31.49	9.28	21.68	31.25	9.58	20.85	29.97	9.12
West South Central	24.93	37.88	12.95	24.43	37.33	12.90	23.73	36.10	12.38	23.98	34.78	10.80	22.75	33.73	10.98	21.85	33.83	11.98	21.08	31.98	10.90
East South Central	25.18	34.93	9.75	24.78	35.03	10.25	23.53	34.55	11.03	23.10	34.48	11.38	21.58	33.30	11.73	21.03	32.65	11.63	20.4	30	9.6
South Atlantic	27.00	32.69	5.69	25.89	31.00	5.11	24.48	29.28	4.80	24.44	28.71	4.27	22.66	27.22	4.57	22.32	26.97	4.64	20.96	29.07	8.11

Table 4: Join Point Regression Analysis: Annual Average Percentage Change in Obesity, 1990-2015 by US State in Non-Hispanic White (NHW) And Non-Hispanic Black (NHB) Women. With 95% confidence intervals and P-values. (Insufficient data available for NHB women in South Carolina).

JP Ob table 4	NHW			NHB			AAPC Difference (NHW-NHB)
State	AAPC	AAPC 95%CI	P-Value	AAPC	AAPC 95% CI	P-Value	
Alabama	3.5	1.5 , 5.6	1.2	2.3	0.8,3.9	0.014	1.2
Arkansas	4	2.5 , 5.6	2.1	1.9	-0.4,4.2	0.087	2.1
Delaware	3.2	2.4 , 3.9	1.2	2	1,2.9	0.005	1.2
Washington DC	2.6	0.4 , 4.8	0.5	2.1	1.2,3	0.003	0.5
Florida	2.7	1.9 , 3.6	1.4	1.3	-0.4,3	0.096	1.4
Georgia	4.3	0.9 , 7.7	1.7	2.6	0,5.4	0.051	1.7
Kentucky	3.2	1.2 , 5.3	-0.1	3.3	1.3,5.3	0.009	-0.1
Louisiana	3	2.1 , 4	0.7	2.3	1,3.6	0.008	0.7
Maryland	3.3	1.5 , 5.2	0.4	2.9	1.5,4.2	0.004	0.4
Mississippi	3.9	1.8 , 6.1	2	1.9	0.9,3	0.006	2
North Carolina	2.9	1 , 4.9	1.3	1.6	-0.7,3.8	0.126	1.3
Oklahoma	3.8	2 , 5.7	1.5	2.3	1.3,3.4	0.003	1.5
South Carolina	3.1	0.7 , 5.5	0.8	2.3	0.9,3.7	0.011	0.8
Tennessee	3.7	0.7 , 6.8	1.1	2.6	0.5,4.7	0.026	1.1
Texas	3.1	0.5 , 5.7	1.1	2	0.5,3.5	0.02	1.1
Virginia	2.7	0.7 , 4.8	0.8	1.9	0.7,3.2	0.012	0.8
West Virginia	3	1.5 , 4.6	1.4	1.6	-0.9,4.2	0.156	1.4

Table 5: Join Point Regression Analysis: Annual Average Percentage Change in Breast Cancer-Specific Mortality 1990-2015 By State in Non-Hispanic White (NHW) And Non-Hispanic Black (NHB) Women. With 95% confidence intervals and P-values. (Insufficient data available for NHB women in South Carolina).

	NHW			NHB			AAPC difference (NHB-NHW)
State	AAPC	AAPC 95%CI	P-Value	AAPC	AAPC 95% CI	P-Value	
Alabama	-7.3	-10.1, -4.4	0.002	-5.1	-7,-3.1	0.002	2.2
Arkansas	-6.9	-8.7,-5.2	< 0.001	-3.5	-6.1,-0.9	0.021	3.4
Delaware	-11.3	-14.9,-7.6	0.001	-10.8	-18.9,-1.8	0.03	0.5
Washington DC	-12.5	-21.3,-2.7	0.025	-9.2	-14.6,-3.5	0.012	3.3
Florida	-10.1	-12.8,-7.3	0.001	-7.7	-8.9,-6.4	< 0.001	2.4
Georgia	-8	-9.8,-6.1	< 0.001	-3.2	-7.1,0.9	0.096	4.8
Kentucky	-7.3	-8.5,-6	< 0.001	-9.4	-14.8,-3.7	0.011	-2.1
Louisiana	-9.7	-12.3,-7	0.001	-6	-10.2,-1.6	0.02	3.7
Maryland	-11.2	-13.3,-9	< 0.001	-6.7	-10.3,-2.9	0.008	4.5
Mississippi	-6.4	-9.2,-3.5	0.004	-5.1	-8.8,-1.2	0.022	1.3
North Carolina	-8.2	-10.4,-5.9	0.001	-6	-10.2,-1.7	0.019	2.2
Oklahoma	-6.4	-7.7,-5	< 0.001	-0.5	-8.8,8.5	0.877	5.9
South Carolina	-8.3	-10.2,-6.3	< 0.001	-	-	-	-
Tennessee	-7.4	-9.9,-4.8	0.001	-6	-11.6,-0.1	0.049	1.4
Texas	-8.2	-10,-6.5	< 0.001	-6.1	-8.4,-3.9	0.002	2.1
Virginia	-9.3	-11.9,-6.7	0.001	-7.8	-12.1,-3.3	0.009	1.5
West Virginia	-6.6	-7.7,-5.4	< 0.001	-6.9	-19.5,7.7	0.245	-0.3

References

Breast cancer statistics. (2021, January 21). Retrieved April 20, 2021, from https://www.wcrf.org/dietandcancer/cancer-trends/breast-cancer-statistics

DeSantis, C. E., Ma, J., Gaudet, M. M., Newman, L. A., Miller, K. D., Goding Sauer, A., . . . Siegel, R. L. (2019). Breast cancer statistics, 2019. *CA Cancer J Clin, 69*(6), 438-451. doi:10.3322/caac.21583

Akinyemiju, T., Moore, J. X., Judd, S., Lakoski, S., Goodman, M., Safford, M. M., & Pisu, M. (2017). Metabolic dysregulation and cancer mortality in a national cohort of Blacks and Whites. *Bmc Cancer, 17*. doi:10.1186/s12885-017-3807-2

Akinyemiju, T., Moore, J. X., Ojesina, A. I., Waterbor, J. W., & Altekruse, S. F. (2016). Racial disparities in individual breast cancer outcomes by hormone-receptor subtype, area-level socio-economic status and healthcare resources. *Breast Cancer Research and Treatment, 157*(3), 575-586. doi:10.1007/s10549-016-3840-x

Apovian, C. M. (2016). Obesity: definition, comorbidities, causes, and burden. *Am J Manag Care, 22*(7 Suppl), s176-185.

Bianchini, F., Kaaks, R., & Vainio, H. (2002). Overweight, obesity, and cancer risk. *Lancet Oncol, 3*(9), 565-574. doi:10.1016/s1470-2045(02)00849-5

Bogdanova, N., Helbig, S., & Dörk, T. (2013). Hereditary breast cancer: ever more pieces to the polygenic puzzle. *Hered Cancer Clin Pract, 11*(1), 12. doi:10.1186/1897-4287-11-12

Chahil, T. J., & Ginsberg, H. N. (2006). Diabetic dyslipidemia. *Endocrinol Metab Clin North Am, 35*(3), 491-510, vii-viii. doi:10.1016/j.ecl.2006.06.002

Collaboration, G. B. o. D. C. (2019). Global, Regional, and National Cancer Incidence, Mortality, Years of Life Lost, Years Lived With Disability, and Disability-Adjusted Life-Years for 29 Cancer Groups, 1990 to 2017: A Systematic Analysis for the Global Burden of Disease Study. *Jama Oncology, 5*(12), 1749-1768. doi:10.1001/jamaoncol.2019.2996

De Pergola, G., & Silvestris, F. (2013). Obesity as a major risk factor for cancer. *J Obes, 2013*, 291546. doi:10.1155/2013/291546

DeSantis, C. E., Ma, J., Gaudet, M. M., Newman, L. A., Miller, K. D., Goding Sauer, A., . . . Siegel, R. L. (2019). Breast cancer statistics, 2019. *CA Cancer J Clin, 69*(6), 438-451. doi:10.3322/caac.21583

Dignam, J. J., Wieand, K., Johnson, K. A., Raich, P., Anderson, S. J., Somkin, C., & Wickerham, D. L. (2006). Effects of obesity and race on prognosis in lymph node-negative, estrogen receptor-negative breast cancer. *Breast Cancer Research and Treatment, 97*(3), 245-254. doi:10.1007/s10549-005-9118-3

Hales, C. M., Carroll, M. D., Fryar, C. D., & Ogden, C. L. (2020). Prevalence of Obesity and Severe Obesity Among Adults: United States, 2017-2018. *NCHS Data Brief*(360), 1-8.

Hunt, B. R., Silva, A., Lock, D., & Hurlbert, M. (2019). Predictors of breast cancer mortality among White and BBlack women in large United States cities: an ecologic study. *Cancer Causes & Control, 30*(2), 149-164. doi:10.1007/s10552-018-1125-x

Jemal, A., Robbins, A. S., Lin, C. C., Flanders, W. D., DeSantis, C. E., Ward, E. M., & Freedman, R. A. (2018). Factors That Contributed to Black-White Disparities in Survival Among Nonelderly Women With Breast Cancer Between 2004 and 2013. *J Clin Oncol, 36*(1), 14-24. doi:10.1200/jco.2017.73.7932

Kim, H. J., Fay, M. P., Feuer, E. J., & Midthune, D. N. (2000). Permutation tests for joinpoint regression with applications to cancer rates. *Stat Med, 19*(3), 335-351. doi:10.1002/(sici)1097-0258(20000215)19:3<335::aid-sim336>3.0.co;2-z

Kolak, A., Kaminska, M., Sygit, K., Budny, A., Surdyka, D., Kukielka-Budny, B., & Burdan, F. (2017). Primary and secondary prevention of breast cancer. *Ann Agric Environ Med, 24*(4), 549-553. doi:10.26444/aaem/75943

Laurent, V., Nieto, L., Valet, P., & Muller, C. (2014). [Adipose tissue and cancer: a high risk tandem]. *Med Sci (Paris), 30*(4), 398-404. doi:10.1051/medsci/20143004013

Majeed, W., Aslam, B., Javed, I., Khaliq, T., Muhammad, F., Ali, A., & Raza, A. (2014). Breast cancer: major risk factors and recent developments in treatment. *Asian Pac J Cancer Prev, 15*(8), 3353-3358. doi:10.7314/apjcp.2014.15.8.3353

McTiernan, A. (2018). Weight, physical activity and breast cancer survival. *Proc Nutr Soc*, *77*(4), 403-411. doi:10.1017/s0029665118000010

Picon-Ruiz, M., Morata-Tarifa, C., Valle-Goffin, J. J., Friedman, E. R., & Slingerland, J. M. (2017). Obesity and adverse breast cancer risk and outcome: Mechanistic insights and strategies for intervention. *CA Cancer J Clin*, *67*(5), 378-397. doi:10.3322/caac.21405

Renehan, A. G., Zwahlen, M., & Egger, M. (2015). Adiposity and cancer risk: new mechanistic insights from epidemiology. *Nat Rev Cancer, 15*(8), 484-498. doi:10.1038/nrc3967

Stevens, G. A., Singh, G. M., Lu, Y., Danaei, G., Lin, J. K., Finucane, M. M., . . . Ezzati, M. (2012). National, regional, and global trends in adult overweight and obesity prevalences. *Popul Health Metr, 10*(1), 22. doi:10.1186/1478-7954-10-22

Sun, Y. S., Zhao, Z., Yang, Z. N., Xu, F., Lu, H. J., Zhu, Z. Y., . . . Zhu, H. P. (2017). Risk Factors and Preventions of Breast Cancer. *Int J Biol Sci, 13*(11), 1387-1397. doi:10.7150/ijbs.21635

Whitman, S., Orsi, J., & Hurlbert, M. (2012). The racial disparity in breast cancer mortality in the 25 largest cities in the United States Response. *Cancer Epidemiology, 36*(5), 498-498. doi:10.1016/j.canep.2012.05.008

Wong, W. F., LaVeist, T. A., & Sharfstein, J. M. (2015). Achieving Health Equity by Design. *JAMA, 313*(14), 1417-1418. doi:10.1001/jama.2015.2434

CHAPTER III: Summary, Public Health Significance, Possible Future Directions

This study was initiated with an aim to better understand the potential contribution of obesity to racial disparities in breast cancer mortality. With an aim to highlight population level dynamics of the chosen parameters, an ecologic approach was chosen with the US census as a framework (states and census regions, divisions).

American Cancer Society SEER-STAT and the CDC BRFSS survey results were tapped as sources for our outcome and exposure data respectively. The Southern United States region was chosen as a focus citing the higher proportions of non-Hispanic Black populations in these states. The background and literature review informed our decisions to examine the mortality data with 5- and 10-year lags to the obesity data and supported the choice of joinpoint regression as the method for analysis with annual average percentage changes as the parameter for comparison.

Visual descriptive examination of population level trends revealed an apparent pattern of wide disparities in obesity prevalence with non-Hispanic Black women having a higher rate as a rule and their non-Hispanic White counterparts experiencing sharper declines in breast cancer mortality. Additional insight afforded by the joinpoint regression analysis added weight to the above findings and highlighted a few states such as Georgia, Maryland and Texas as populations that may benefit from further studies and targeted risk reduction interventions.

Public health significance of thesis

With obese breast cancer patients showing several detrimental prognostic factors, weight reduction/ management of obesity is being widely explored in long-term observational studies as a mortality-reducing measure. Efforts to reduce or re-distribute adiposity have been targeted especially at obese post-menopausal women diagnosed with breast cancer who have a higher recurrence and mortality rate. (Picon-Ruiz, Morata-Tarifa, Valle-Goffin, Friedman, & Slingerland, 2017)

This study found several southern US states with slow declining rates of mortality in Non-Hispanic Black women occurring alongside sharply rising obesity rates that supports the above hypotheses at a population level. Moreover, these insights may be used to identify states with high-risk communities in need, help with advocacy for policy changes and allocation of resources for targeted risk-reducing interventions. Knowledge of minority populations experiencing increased mortality is vital to ensure cultural sensitivity and community buy-in of the interventions.

Strengths, limitations, and possible future directions

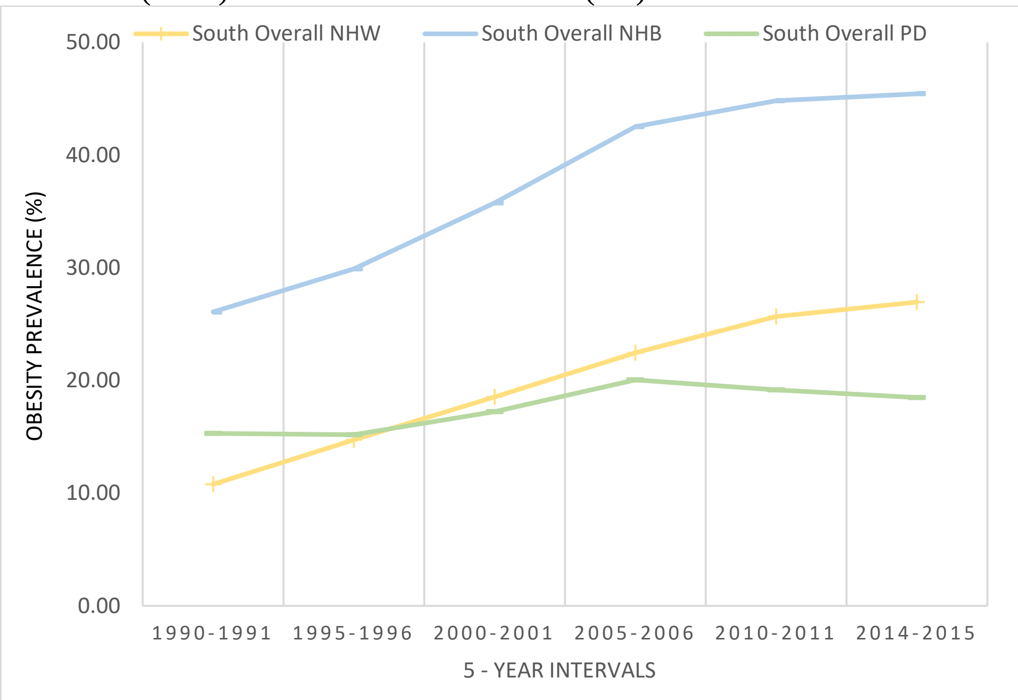
We acknowledge several limitations of the methods used in this study. The source of the exposure data i.e., the Behavioral Risk Factor Surveillance system is a telephone-based survey that relies on self-reported parameters. Weight is likely to be underreported whereas height is likely to be overreported by the general population – however, the wide sampling and stratification are measures built into the survey to help reduce bias.

The ecologic design restricts itself to a large-scale examination of health outcomes. This precludes any individual level correlation and cannot be used to infer a cause-and-effect relationship between the exposure and outcome data. However, this design does allow an initial examination of the health status and needs of communities, which was the intended goal. Ecologic studies are best employed as a means of generating hypotheses rather than deriving definitive information about associations between risk factors and health outcomes. A prospective cohort design would be the ideal format to definitively explore individual level risk for breast cancer mortality in women with obesity. Studies of obesity in high-risk groups such as post-menopausal women with breast cancer and those with certain tumor hormone receptor status categorized by race and ethnicity may help elucidate why these individuals remain at a disproportionately higher breast cancer recurrence and mortality risk.

Appendix : Trend Visualization Figures

Fig 3 - Trends for the Southern region, over all

(i) 2-year Avg Obesity Prevalence (%) in Non-Hispanic White (NHW) and Non-Hispanic Black women (NHB) and Prevalence Difference (PD) 1990-2015



(ii) 2-year Avg Breast Cancer Mortality rate (per 100,1000) in Non-Hispanic White (NHW) and Non-Hispanic Black women (NHB) and Rate difference (RD), 1990-2016

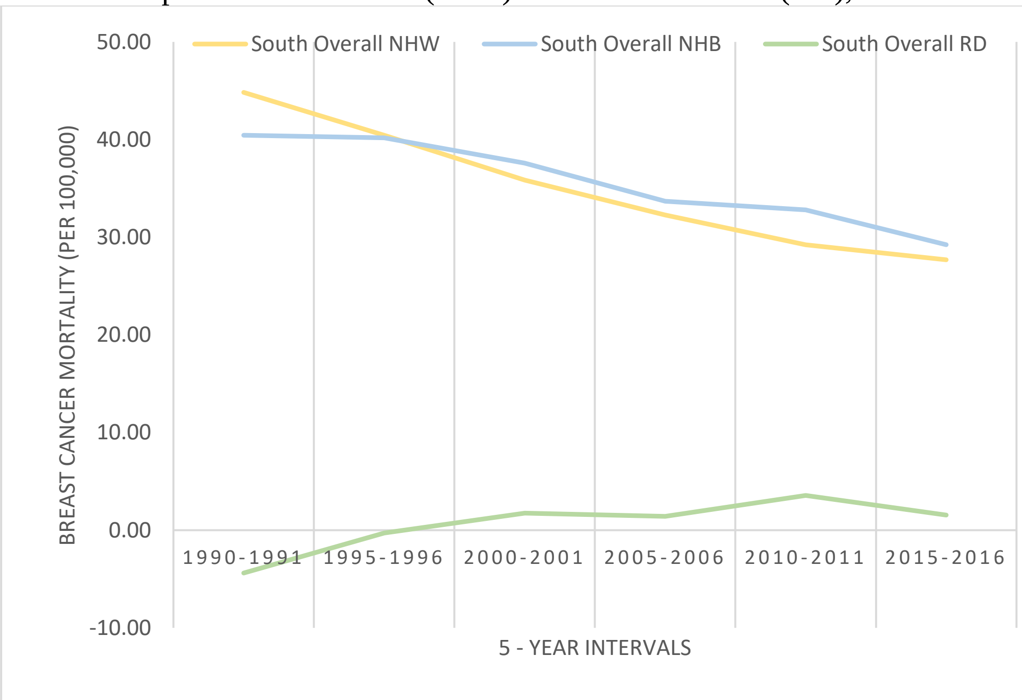
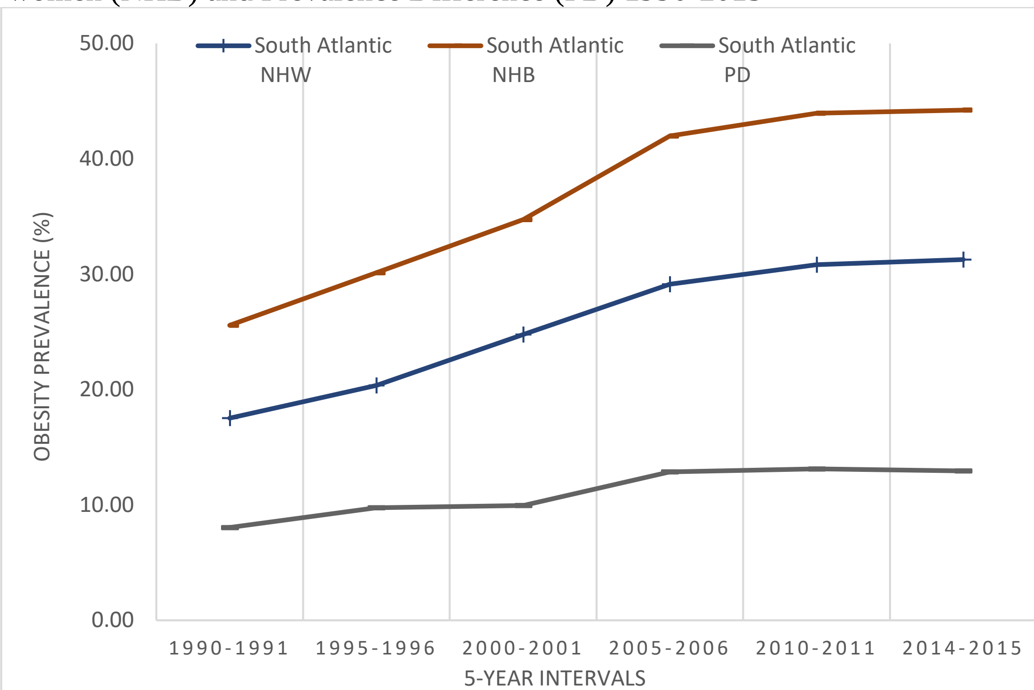


***Fig 4 -Trends for South Atlantic division* (DE, DC, FL, GA, MD, NC, SC, VA, WV)**

(i) 2-year Avg Obesity Prevalence (%) in Non-Hispanic White (NHW) and Non-Hispanic Black women (NHB) and Prevalence Difference (PD) 1990-2015



(ii) 2-year Avg Breast Cancer Mortality rate (per 100,1000) in Non-Hispanic White (NHW) and Non-Hispanic Black women (NHB) and Rate difference (RD) , 1990-2016

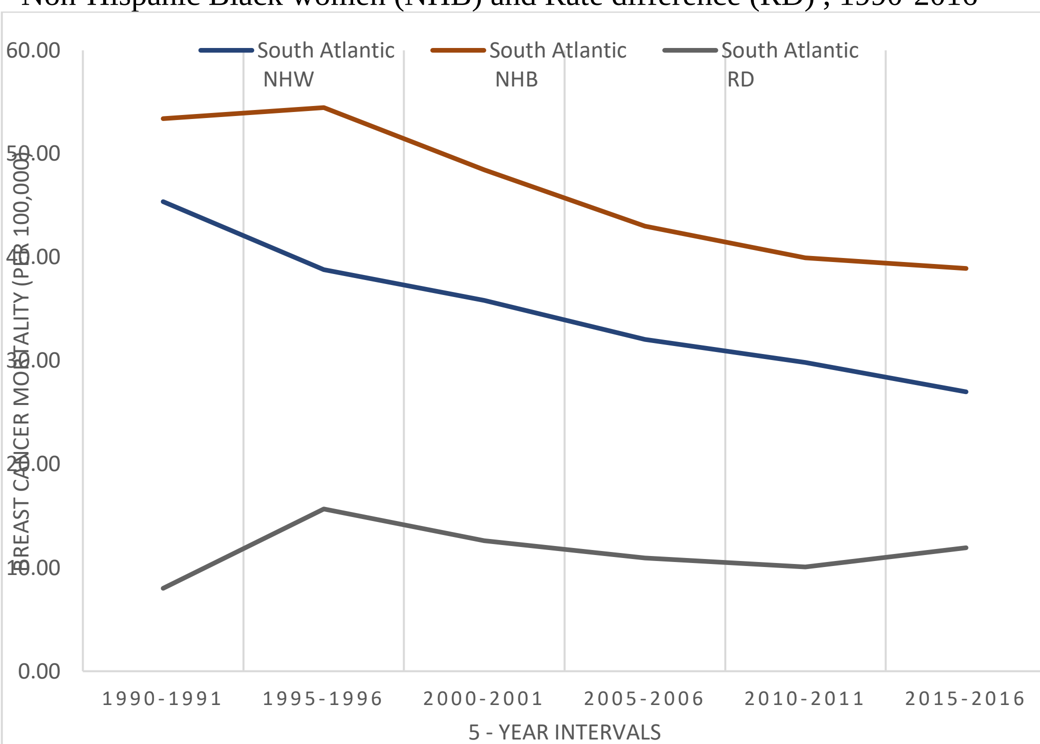
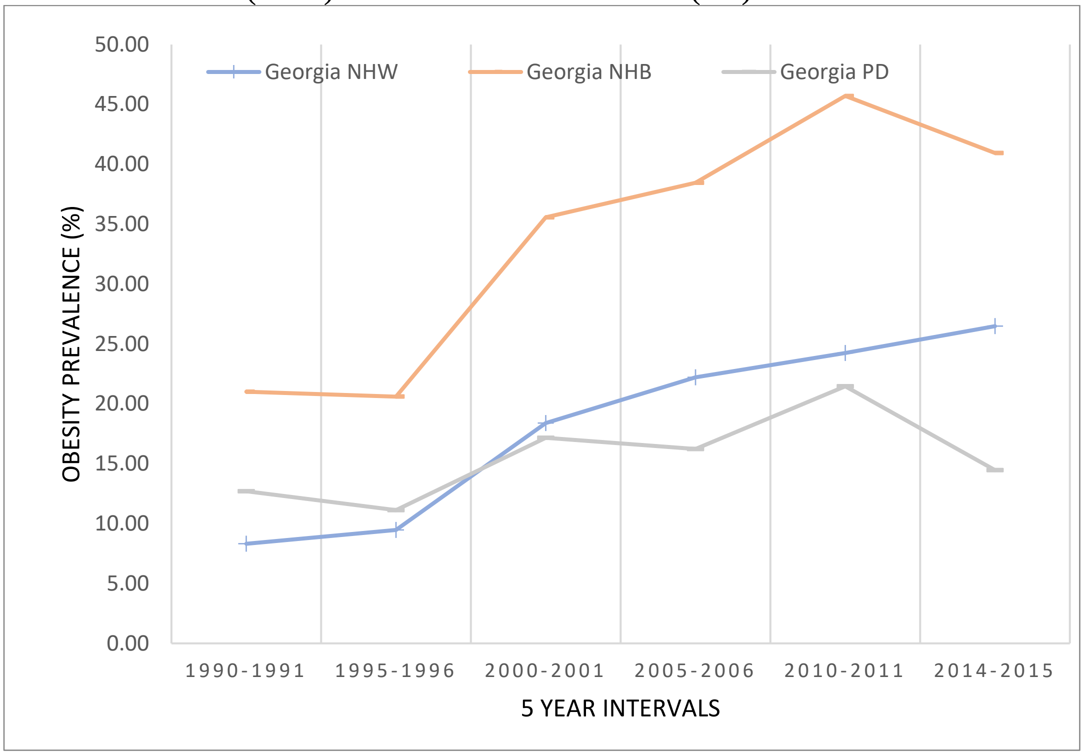


Fig 4a - Trends for ***Georgia***

(i) 2-year Avg Obesity Prevalence (%) in Non-Hispanic White (NHW) and Non-Hispanic Black women (NHB) and Prevalence Difference (PD) 1990-2015



(ii) 2-year Avg Breast Cancer Mortality rate (per 100,1000) in Non-Hispanic White (NHW) and Non-Hispanic Black women (NHB) and Rate difference (RD), 1990-2016

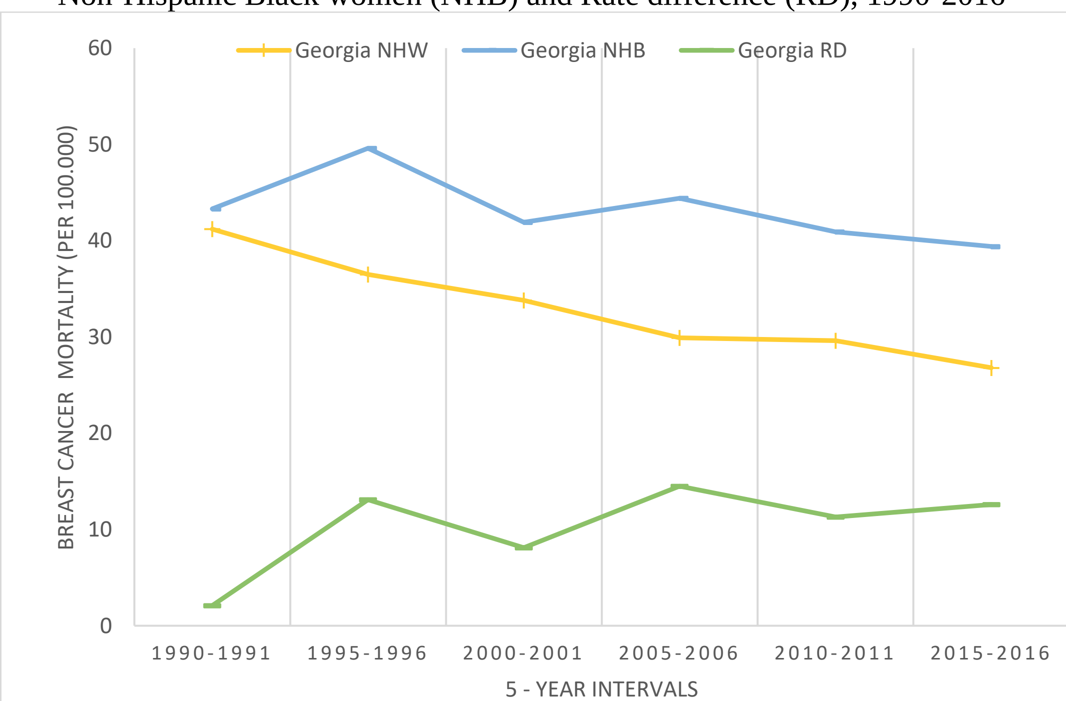
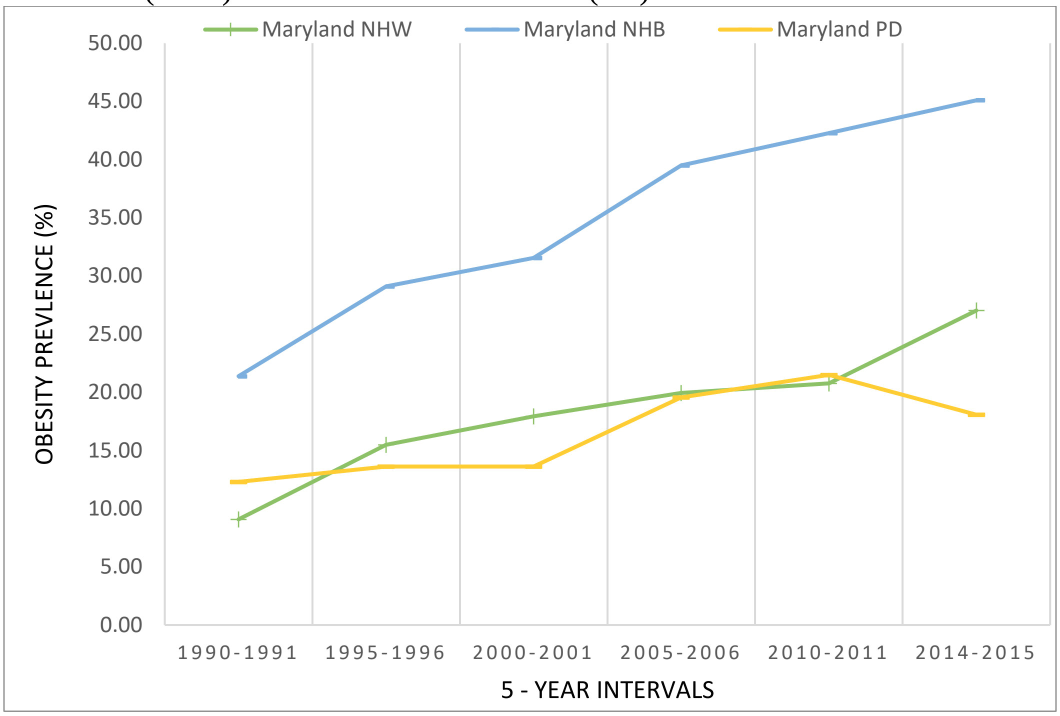


Fig 4b - Trends for Maryland

(i) 2-year Avg Obesity Prevalence (%) in Non-Hispanic White (NHW) and Non-Hispanic Black women (NHB) and Prevalence Difference (PD) 1990-2015



(ii) 2-year Avg Breast Cancer Mortality rate (per 100,1000) in Non-Hispanic White (NHW) and Non-Hispanic Black women (NHB) and Rate difference (RD) 1990-2016

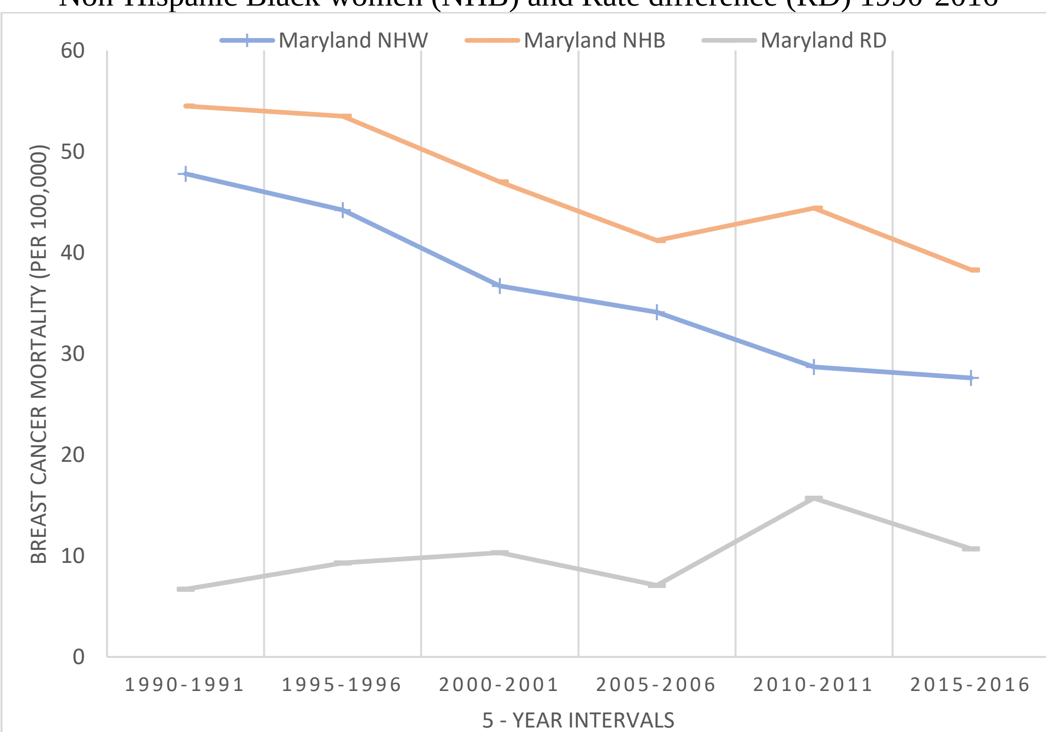
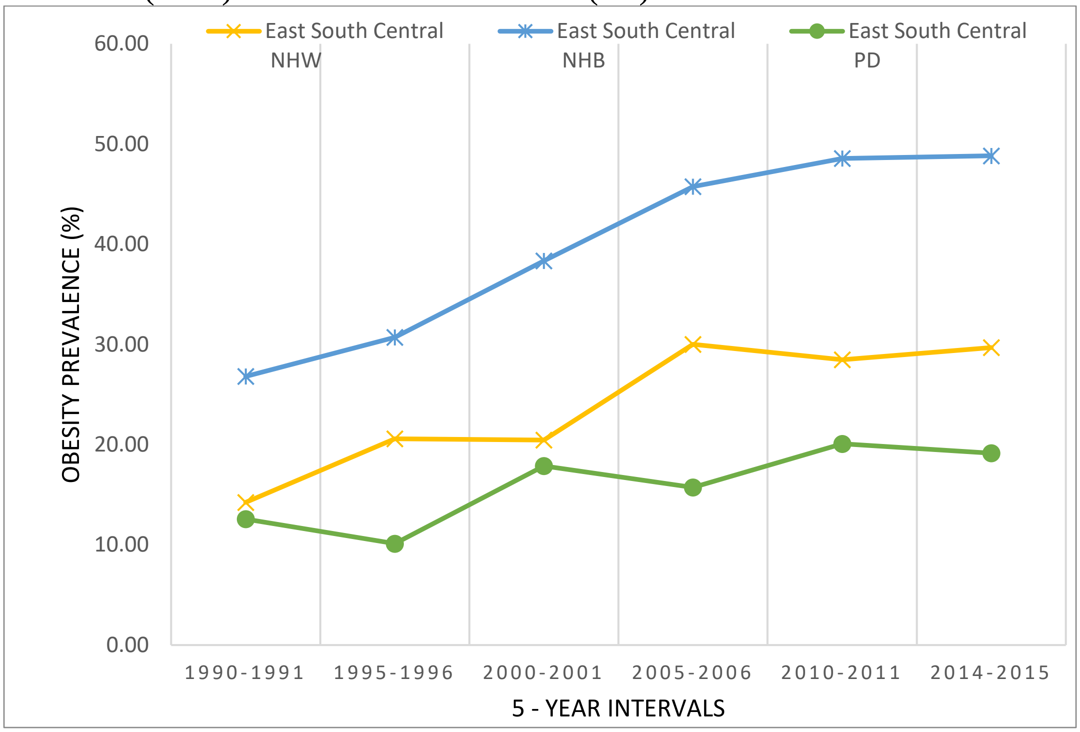


Fig 5 - Trends for East South-Central Division (AL, KY, MS, TN)

(i) 2-year Avg Obesity Prevalence (%) in Non-Hispanic White (NHW) and Non-Hispanic Black women (NHB) and Prevalence Difference (PD) 1990-2015



(ii) 2-year Avg Breast Cancer Mortality rate (per 100,1000) in Non-Hispanic White (NHW) and Non-Hispanic Black women (NHB) and Rate difference (RD) 1990-2016

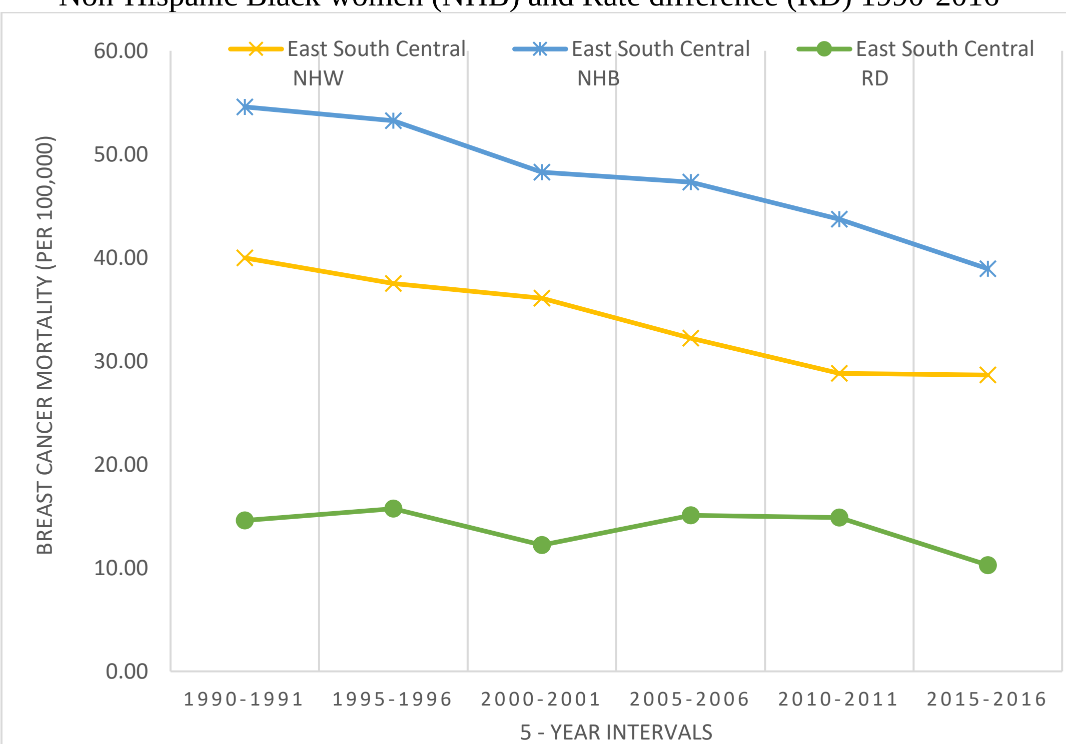
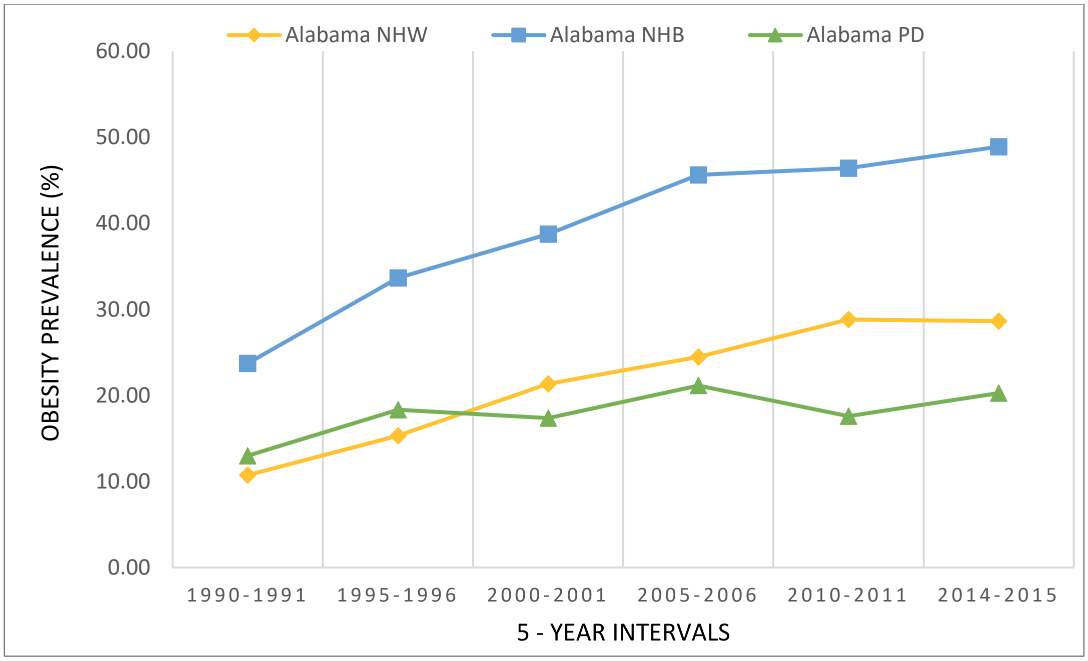


Fig 5a - Trends for ***Alabama***

(i) 2-year Avg Obesity Prevalence (%) in Non-Hispanic White (NHW) and Non-Hispanic Black women (NHB) and Prevalence Difference (PD) 1990-2015



(ii) 2-year Avg Breast Cancer Mortality rate (per 100,1000) in Non-Hispanic White (NHW) and Non-Hispanic Black women (NHB) and Rate difference (RD) 1990-2016

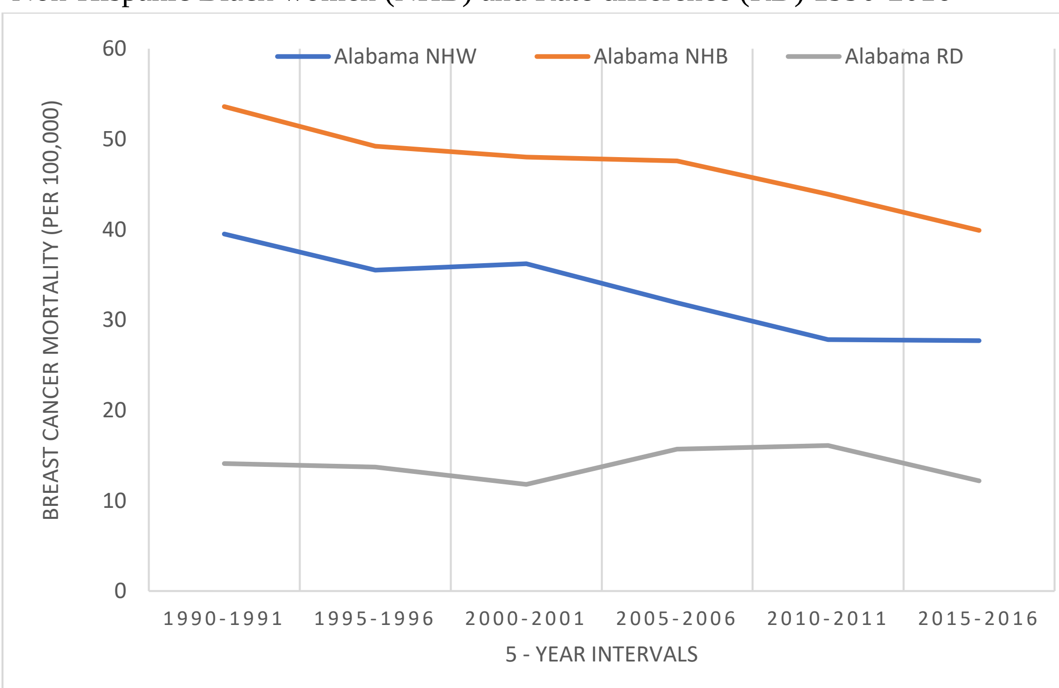
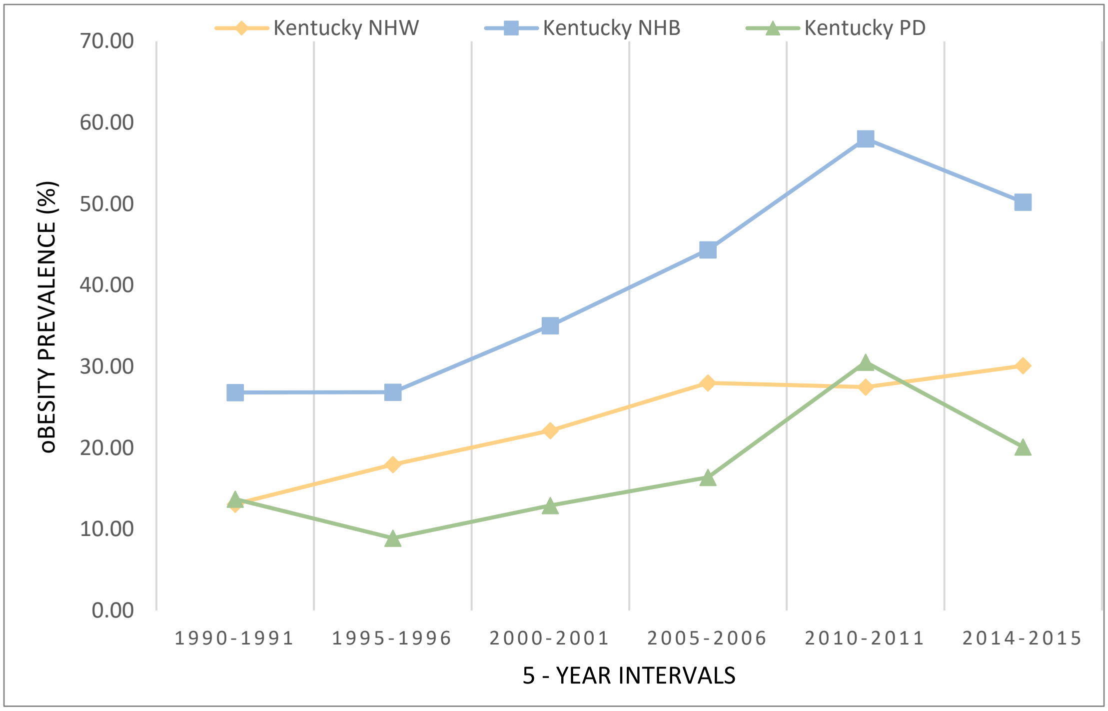


Fig 5b – Trends for ***Kentucky***

(i) 2-year Avg Obesity Prevalence (%) in Non-Hispanic White (NHW) and Non-Hispanic Black women (NHB) and Prevalence Difference (PD) 1990-2015



(ii) 2-year Avg Breast Cancer Mortality rate (per 100,1000) in Non-Hispanic White (NHW) and Non-Hispanic Black women (NHB) and Rate difference (RD) 1990-2016

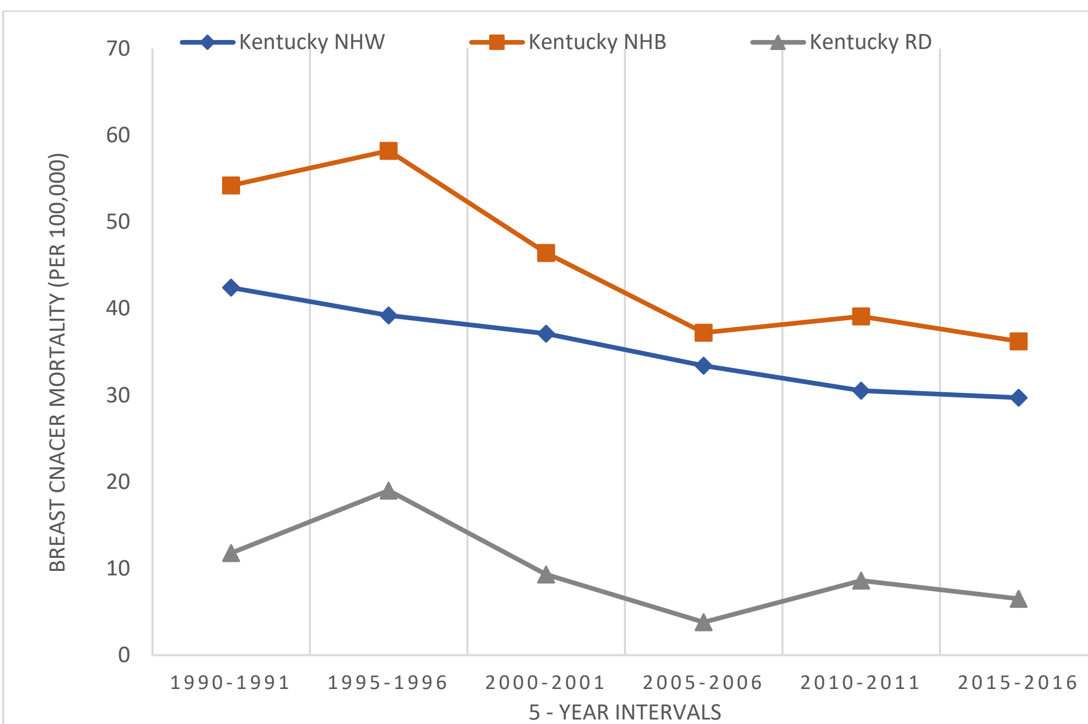
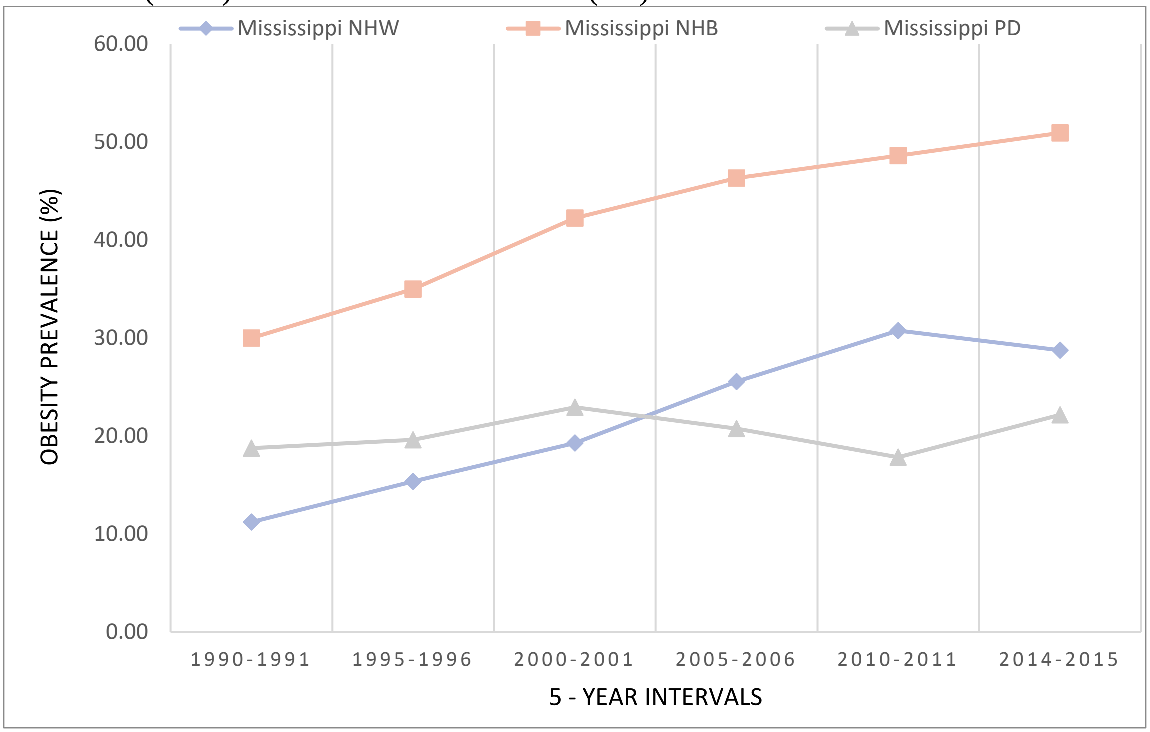


Fig 5c - Trends for ***Mississippi***

(i) 2-year Avg Obesity Prevalence (%) in Non-Hispanic White (NHW) and Non-Hispanic Black women (NHB) and Prevalence Difference (PD) 1990-2015



(ii) 2-year Avg Breast Cancer Mortality rate (per 100,1000) in Non-Hispanic White (NHW) and Non-Hispanic Black women (NHB) and Rate difference (RD) 1990-2016

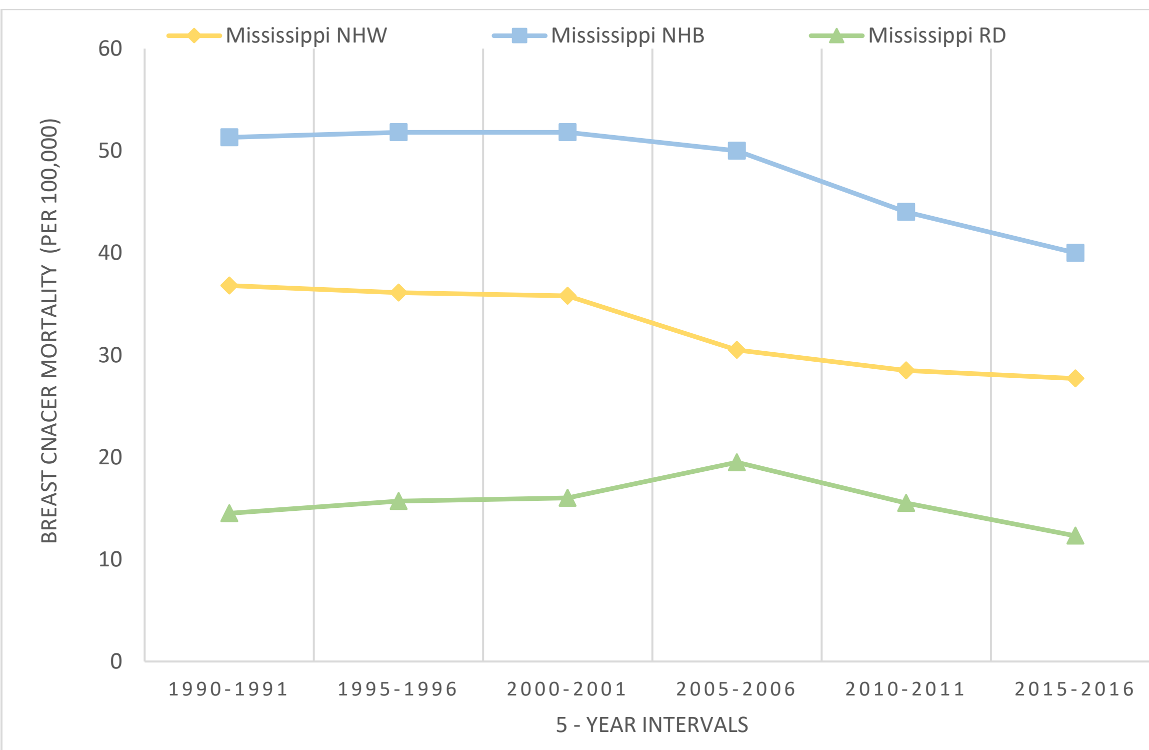
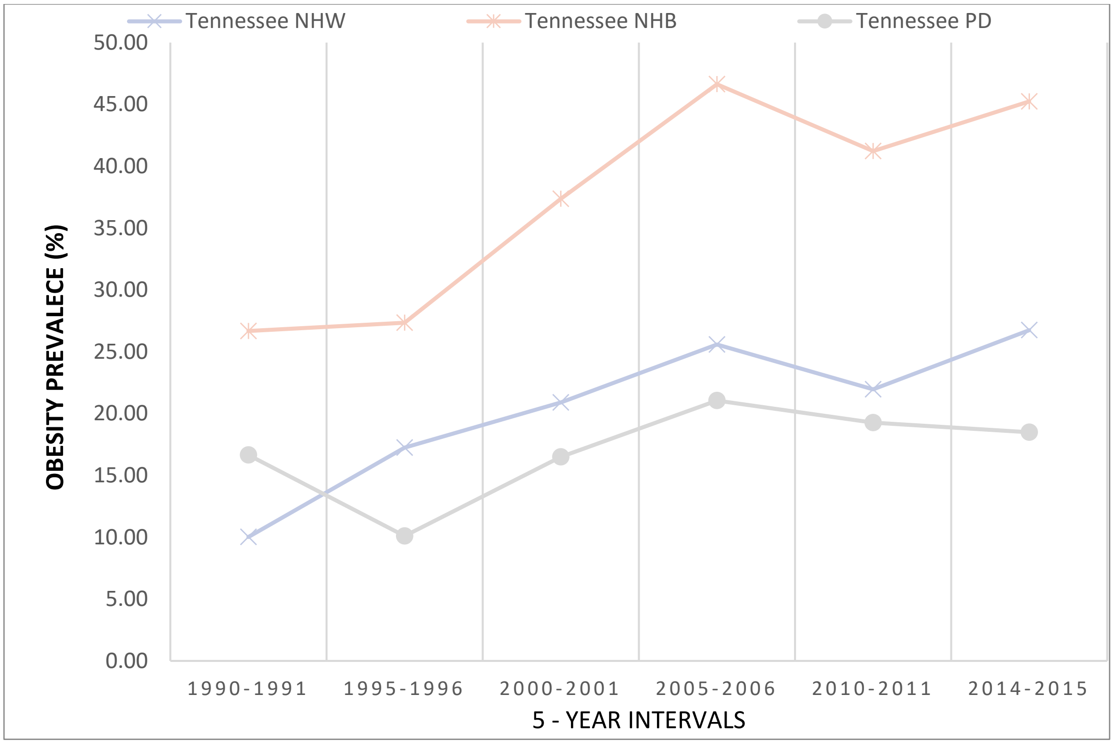


Fig 5d - Trends for ***Tennessee***

(i) 2-year Avg Obesity Prevalence (%) in Non-Hispanic White (NHW) and Non-Hispanic Black women (NHB) and Prevalence Difference (PD) 1990-2015



(ii)2-year Avg Breast Cancer Mortality rate (per 100,1000) in Non-Hispanic White (NHW) and Non-Hispanic Black women (NHB) and Rate difference (RD) 1990-2016

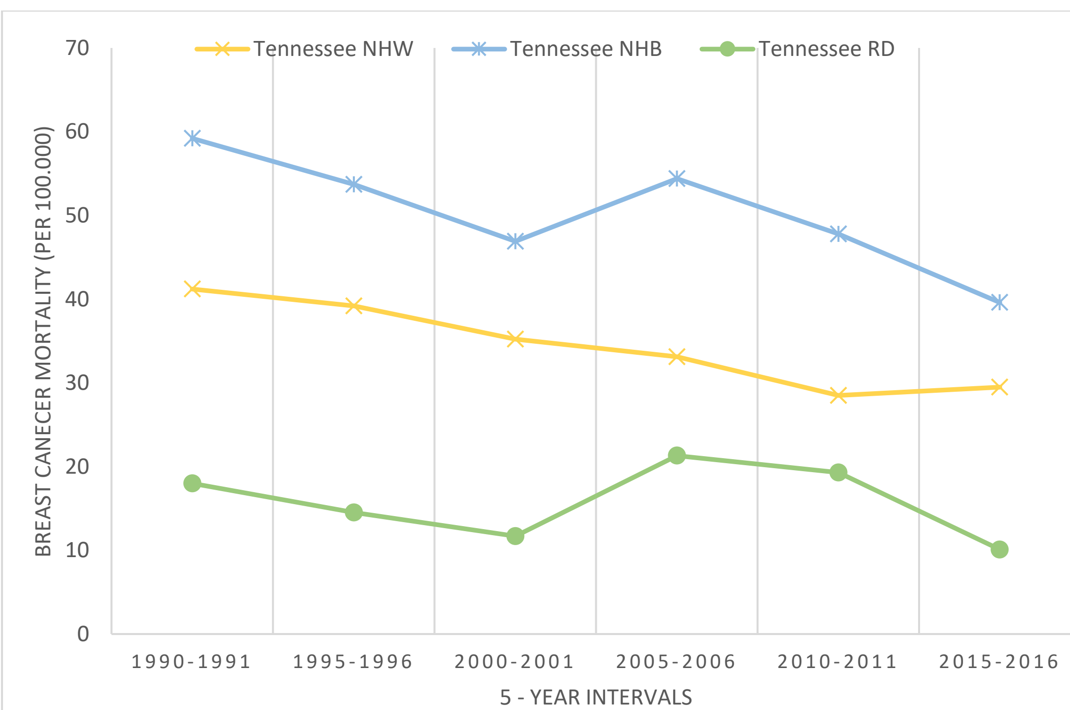
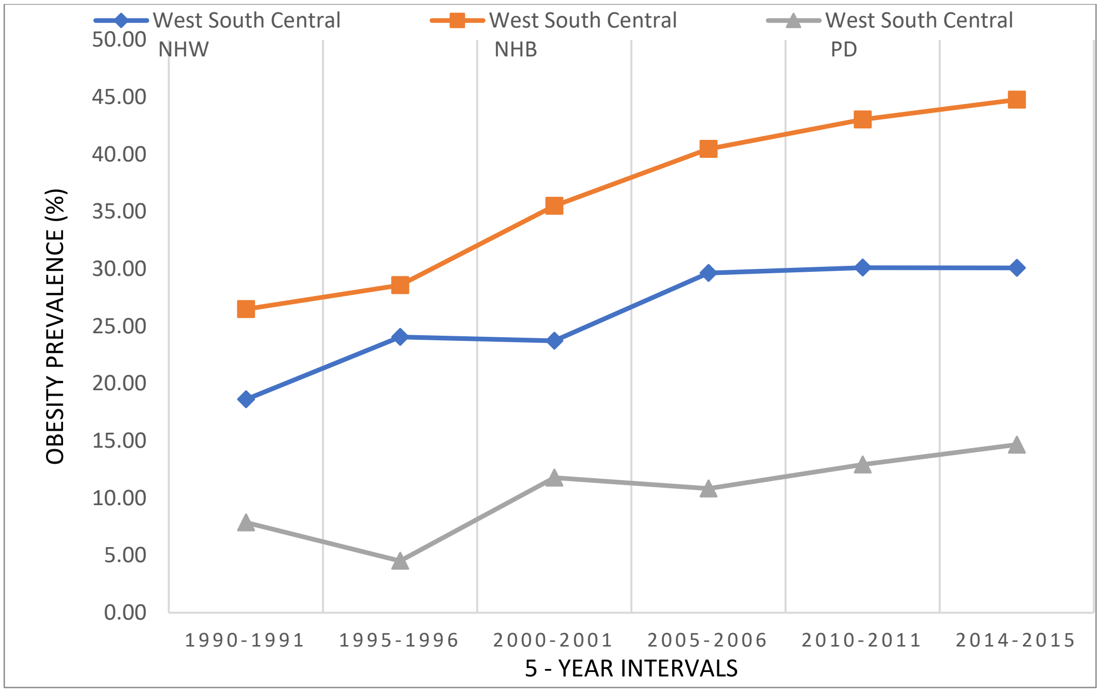


Fig 6 - Trends for West South-Central division (AR LA OK TX)

(i) 2-year Avg Obesity Prevalence (%) in Non-Hispanic White (NHW) and Non-Hispanic Black women (NHB) and Prevalence Difference (PD) 1990-2015



(ii) 2-year Avg Breast Cancer Mortality rate (per 100,1000) in Non-Hispanic White (NHW) and Non-Hispanic Black women (NHB) and Rate difference (RD) 1990-2016

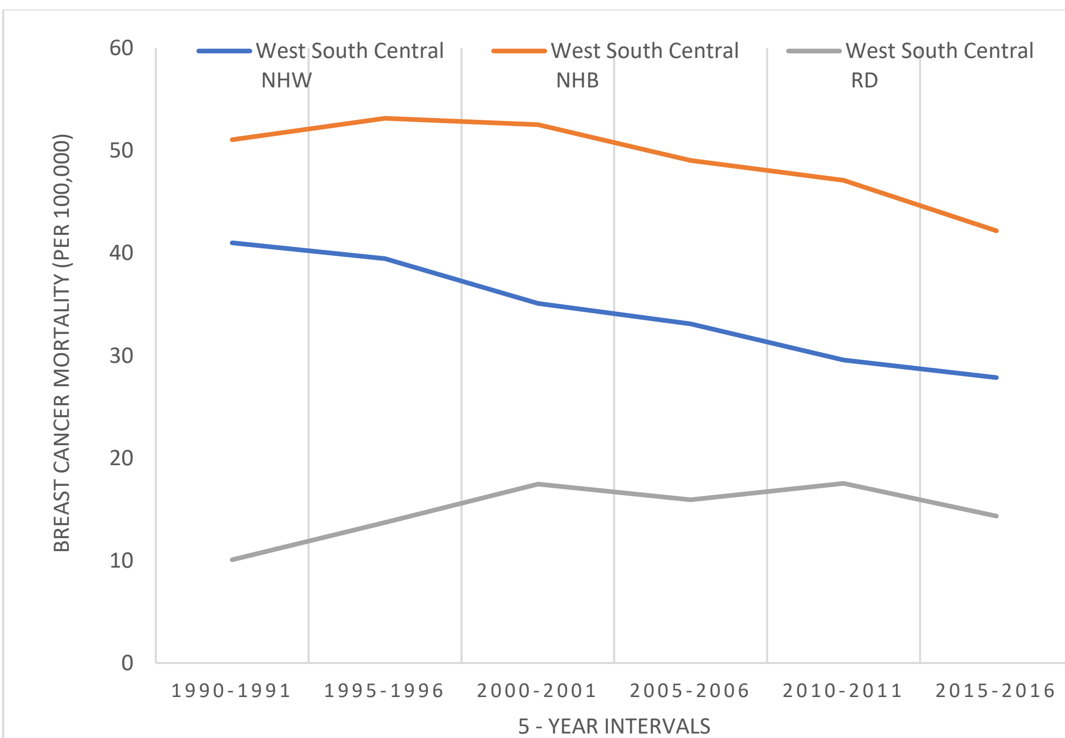
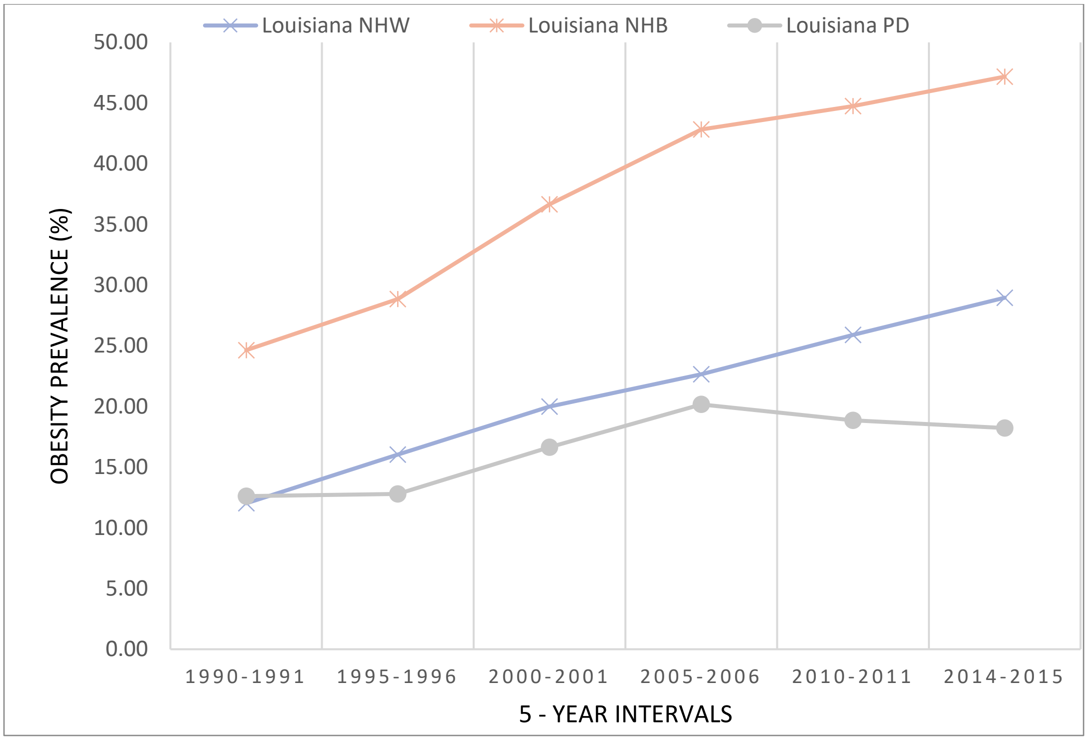


Fig 6a - Trends for ***Louisiana***

(i) 2-year Avg Obesity Prevalence (%) in Non-Hispanic White (NHW) and Non-Hispanic Black women (NHB) and Prevalence Difference (PD) 1990-2015



(ii)2-year Avg Breast Cancer Mortality rate (per 100,1000) in Non-Hispanic White (NHW) and Non-Hispanic Black women (NHB) and Rate difference (RD) 1990-2016

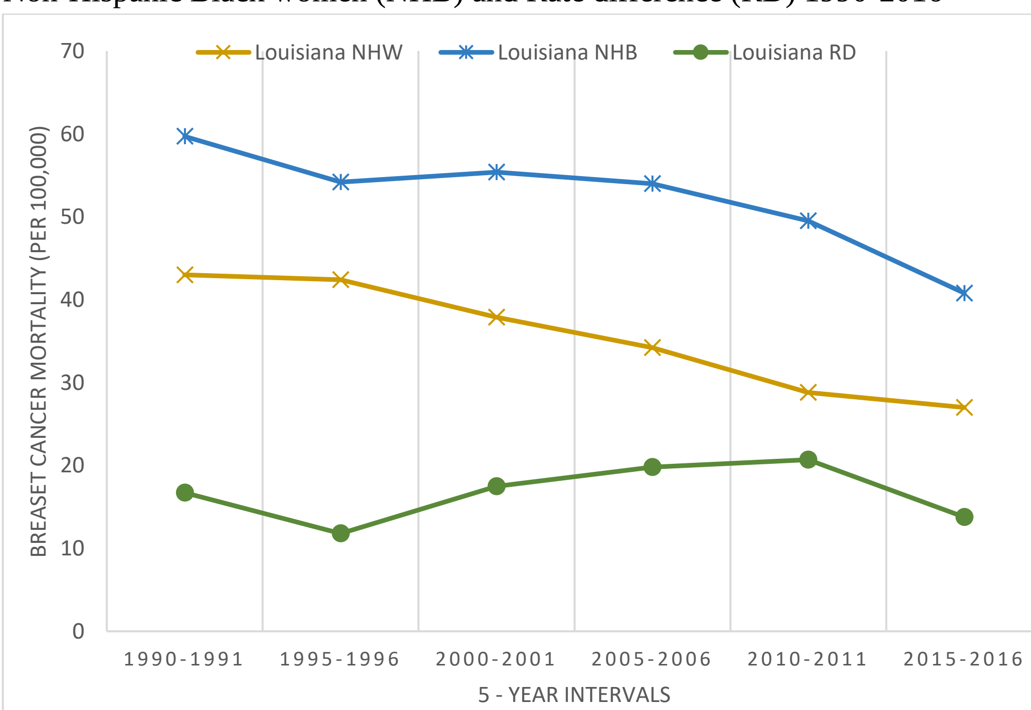
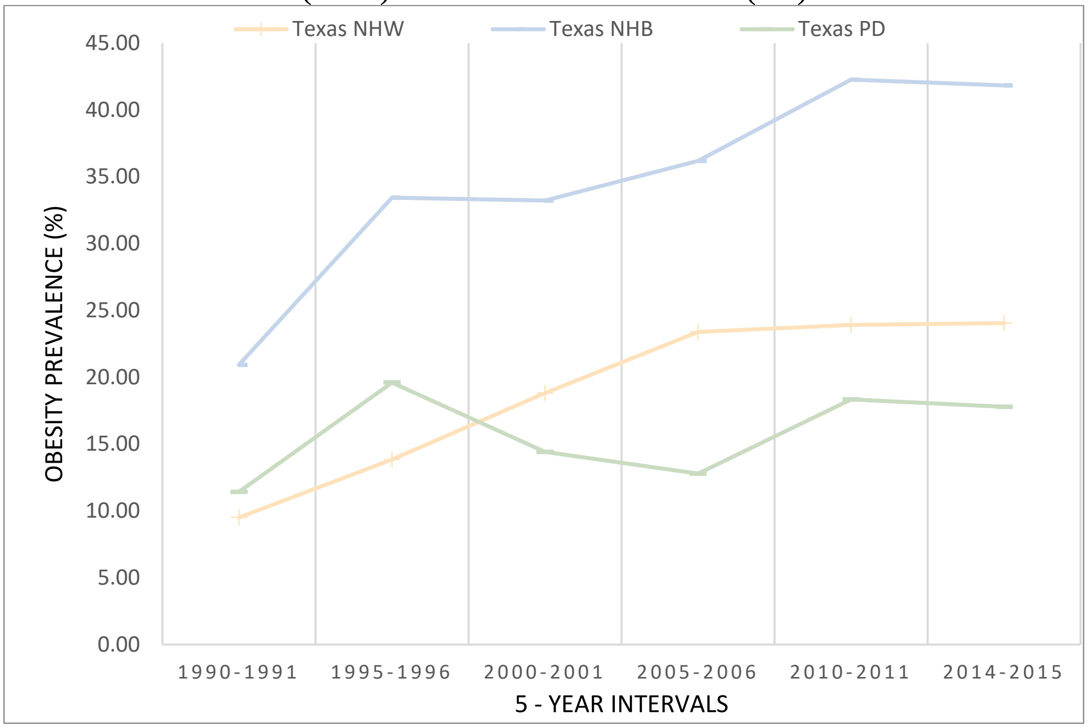


Fig 6b - Trends for Texas

(i) 2-year Avg Obesity Prevalence (%) in Non-Hispanic White (NHW) and Non-Hispanic BlackBlack women (NHB) and Prevalence Difference (PD) 1990-2015



(ii)2-year Avg Breast Cancer Mortality rate (per 100,1000) in Non-Hispanic White (NHW) and Non-Hispanic Black women (NHB) and Rate difference (RD) 1990-2016