



Mediation of Racial Disparities in Breast Cancer Multigene Prognostic Score by Area level Socioeconomic Position, Insurance Status and Rurality.

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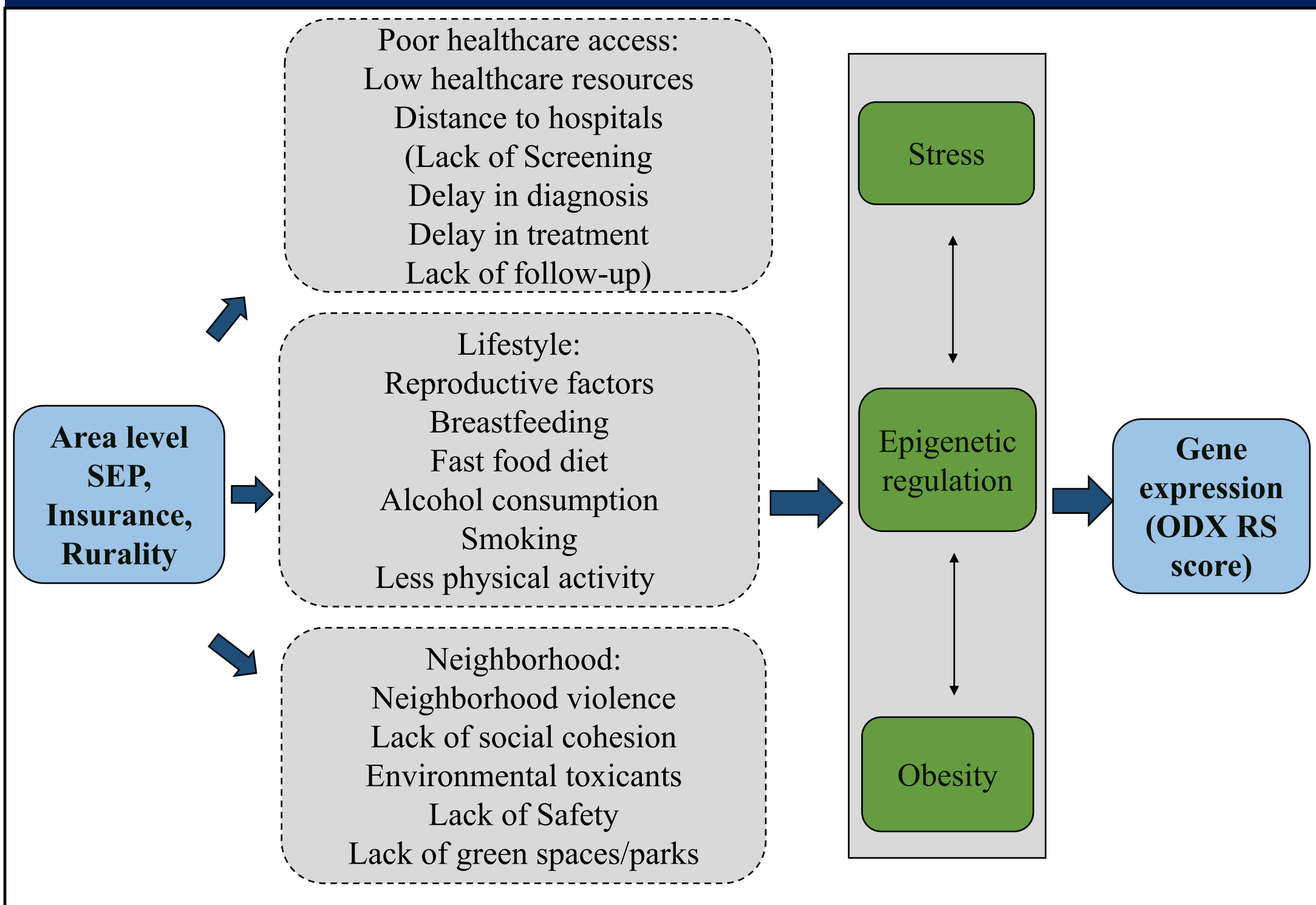
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BACKGROUND

- Oncotype Dx Breast Recurrence Score (ODX RS) is the most widely used multigene prognostic score used to quantify breast cancer (BC) recurrence risk¹.
- Multiple studies have shown that NHB women tend to have higher ODX RS scores compared to NHW women^{2,3}.
- Growing evidence has shown that social determinants of health influence tumor biology; however, no studies have quantified the relative contributions of these factors pertaining to breast cancer recurrence risk⁴.
- This study aims to quantify the extent of mediation by social determinants of health including area level socioeconomic position (SEP), insurance, and rurality in explaining the high recurrence scores in different racial/ethnic groups.

Figure 1: Theoretical Framework



OBJECTIVE

- This study aims to determine whether area level SEP, insurance status and rurality mediates racial/ethnic differences in BC recurrence risk among estrogen receptor positive (ER+) and Human epidermal growth factor2 (HER2-) negative BC patients.

METHODS

Study Design: Retrospective observational study

Data Source: Surveillance, Epidemiology and End Results Oncotype Dx database.

Study population: Women ages ≥ 18 diagnosed with an early stage (I-II) ER (+) HER2

(-) breast cancer (BC) between 2004-2015 were included in the study

RESULTS

Table 1: Descriptive Characteristics of Women with a Diagnosis of Incident, Invasive stage I to II Breast Cancer in the Surveillance, Epidemiology, and End Results Program by Race/Ethnicity, 2004-2015

Characteristics at BC Diagnosis	Non-Hispanic White (NHW)		Non-Hispanic Black (NHB)		Non-Hispanic American Indian or Alaskan Native (NHAIAN)		Non-Hispanic Asian or Pacific Islander (NHAPI)		Hispanic		P value
	n	%	n	%	n	%	n	%	n	%	
	(n= 51158)		(n= 5380)		(n= 274)		(n= 6017)		(n= 6310)		
Age	58.33 [10.29]		57.13 [10.82]		56.74[9.69]		54.84[10.54]		55.48[10.66]		<0.01
Insurance status											<0.01
Insured	47967	(93.8)	4398	(81.7)	214	(78.1)	5329	(88.6)	4829	(76.5)	
Medicaid or Uninsured	3191	(6.2)	982	(18.3)	60	(21.9)	688	(11.4)	1481	(23.5)	
Rurality											<0.01
Rural	5781	(11.3)	366	(6.8)	61	(22.3)	216	(3.6)	255	(4.0)	
Urban	45377	(88.7)	5014	(93.2)	213	(77.7)	5801	(96.4)	6055	(96.0)	
Marital status											<0.01
Married	33618	(65.7)	2103	(39.1)	133	(48.5)	4220	(70.1)	3724	(59.0)	
Not Married	15661	(30.6)	3059	(56.9)	123	(44.9)	1618	(26.9)	2329	(36.9)	
Oncotype Dx group											<0.01
High	6973	(13.6)	939	(17.5)	49	(17.9)	868	(14.4)	874	(13.9)	
Low	44185	(86.4)	4441	(82.5)	225	(82.1)	5149	(85.6)	5436	(86.1)	
Socioeconomic position											<0.01
1 (Highest)	13145	(25.7)	502	(9.3)	60	(21.9)	1753	(29.1)	649	(10.3)	
2	12670	(24.8)	1272	(23.6)	61	(22.3)	575	(9.6)	877	(13.9)	
3	9948	(19.4)	835	(15.5)	44	(16.1)	1635	(27.2)	1280	(20.3)	
4	9766	(19.1)	1655	(30.8)	50	(18.2)	1710	(28.4)	2259	(35.8)	
5 (Lowest)	5629	(11.0)	1116	(20.7)	59	(21.5)	344	(5.7)	1245	(19.7)	

Table 2: Results from Multivariable Logistic Models showing Association of Race/Ethnicity with the Odds of High Oncotype Dx Score

High Oncotype DX Score vs Low/Intermediate Score	Crude model		Adjusted model			
	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
NHW	1[Reference]	NA	1[Reference]	NA	1[Reference]	NA
Hispanic	1.0 [0.9,1.1]	0.63	1.0 [0.9,1.1]	0.61	1.1 [0.8,1.6]	0.51
NHAIAN	1.4 [1.0,1.9]	0.04	1.4 [1.0,1.9]	0.04	1.6 [0.7,3.3]	0.19
NHAPI	1.1 [1.0,1.2]	0.09	1.1 [1.0,1.2]	0.07	1.3 [0.9,1.8]	0.19
NHB	1.3 [1.2,1.4]	<0.01	1.3 [1.2,1.4]	<0.01	1.3 [0.9,1.7]	0.13

Table 3: Results from Multivariable Logistic Model Associating Race/Ethnicity with Mediators; County level Socioeconomic Position, Insurance Status and Rurality

	Odds of Lowest Socioeconomic Position		Odds of being Uninsured/ Medicare covered		Odds of living in Rural Area	
	Reference		Reference		Reference	
NHW						
Hispanic	2.1 [1.9,2.2]	<0.01	4.3 [4.0,4.6]	<0.01	0.35 [0.3,0.4]	<0.01
NHAIAN	2.3 [1.7,3.0]	<0.01	3.6 [2.6,4.8]	<0.01	2.37 [1.8,3.1]	<0.01
NHAPI	0.5 [0.5,0.5]	<0.01	2.0 [1.8,2.1]	<0.01	0.31 [0.3,0.4]	<0.01
NHB	2.2 [2.0,2.3]	<0.01	2.5 [2.3,2.7]	<0.01	0.6 [0.5,0.7]	<0.01

Table 4: Causal Mediation Analyses of Indirect and Direct Effects of Race/Ethnicity on Risk of High Oncotype Dx score by Socioeconomic Position (SEP), Insurance and Rurality

	Mediation by Socioeconomic Position	
	NDE	0.8
NHB	NIE	1.0
	TE	0.7
	PM:	17% [-0.19, -0.08]
	NDE	1.4
NHAIAN	NIE	1.0
	TE	1.4
	PM:	15% [-0.63, 0.23]
	NDE	1.1
NHAPI	NIE	1.0
	TE	1.1
	PM:	20% [-0.36,0.56]
	NDE	1.0
Hispanic	NIE	1.0
	TE	1.0
	PM:	7% [-6.58, 1.40]
	NDE	1.0

Abbreviations: NDE, Natural Direct Effect; NIE, Natural Indirect Effects ; TE, Total Effect; PM, Proportion Mediated [NDE*(NIE-1)]/(NDE*NIE-1)]

METHODS

Statistical Analysis

- The primary outcome is BC recurrence risk measured by high Oncotype DX recurrence score (ODX RS), a multigene prognostic tool for BC. BC patients were categorized into two categories: not high risk (RS, 0-25) and high risk (25-100), as defined by TAILORx study¹.
- Area level SEP, insurance status (proxy of individual level SEP) and census tract level rurality were evaluated as mediators.
- SEP was calculated using principal component analysis on four county level variables (income, poverty, education and unemployment). Health insurance status was categorized as insured and uninsured or Medicaid. Rurality was defined using a binary classification Rural-Urban Commuting Area measure in this study.
- We conducted mediation analyses using product method approach proposed by Baron and Kenny and later by Vanderweele⁵.

Key Findings

- A total of 69139 women diagnosed with node negative early-stage BC were included in this analysis.
- NHB (OR, 1.3[95% CI, 1.2- 1.4]) and NHAIAN women (OR, 1.4 [95% CI, 1.0- 1.9]) were thirty percent more likely to have a high ODX RS than NHW women
- NHB, NHAIAN and Hispanic women had a two-fold greater odds of living in neighborhoods classified as lowest SEP quintile; had more than two-fold increased odds of being uninsured and residing in urban areas compared to NHW and Non-Hispanic Asian Pacific Islander (NHAPI).
- Association of race/ethnicity and odds of high ODX RS was attenuated for NHB women [NHB: OR 1.26 (95% CI, 0.92- 1.70) after adjusting for SEP, insurance status and rurality as a mediator.
- The proportion effect mediation was statistically significant for NHB patients with 17% mediation by area level SEP, insurance and rurality (PM: 17%, 95% CI: -0.19, -0.08) but not for the other racial/ethnic group.

Discussion

- Although we saw a modest level of mediation, it is still meaningful given the gene-environment interactions are complex and more intricate to explain
- It is well studied that one of the ways neighborhood socioeconomic disadvantage adversely affects tumor biology is with its correlation with increasing obesity. Recent study by Gordon et al confirmed this by finding that unit increase in insulin resistance increases the odds of high ODX RS score by thirty percent compared to low ODX RS score.
- Future studies are warranted to further dissect the role of social determinants of health in the disparity of ODX RS score.

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