

Supplementary Online Content

Hoskins KF, Danciu OC, Ko NY, Calip GS. Association of race/ethnicity and the 21-gene recurrence score with breast cancer-specific mortality among US women. *JAMA Oncol*. Published online January 21, 2021. doi:10.1001/jamaoncol.2020.7320

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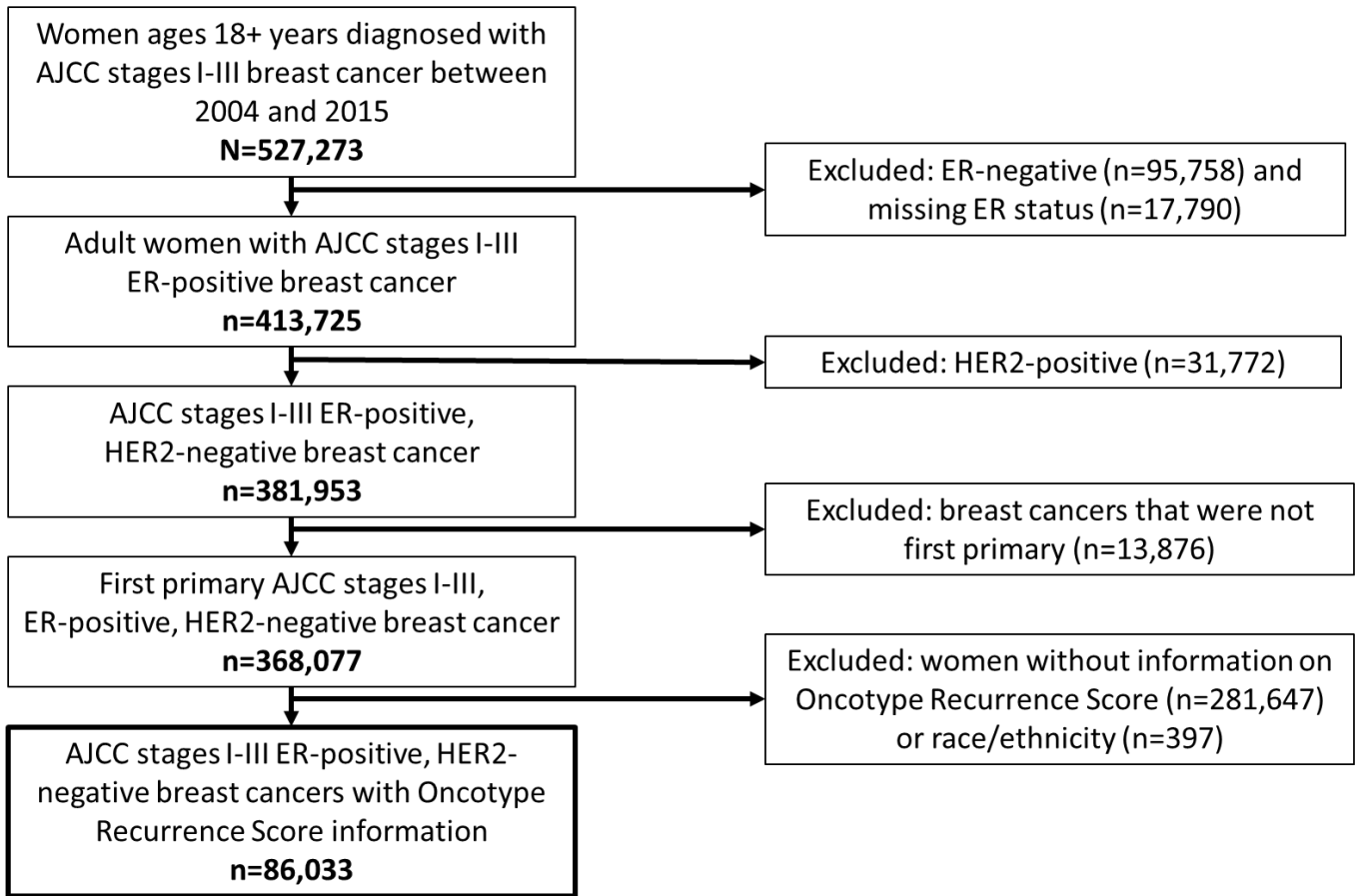
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This supplementary material has been provided by the authors to give readers additional information about their work.

eFigure 1. CONSORT diagram of study cohort selection



eTable 1. Characteristics of study participants

	Recurrence Score 0-10 (n=18,214)		Recurrence Score 11-25 (n=56,050)		Recurrence Score >25 (n=12,166)		P^a
	n	(%)	n	(%)	n	(%)	
Age, years							
Median (interquartile range)	60	(51-67)	57	(49-65)	58	(50-65)	<0.01
18-39	398	(13.2)	1,987	(66.1)	620	(20.6)	<0.01
40-49	3,211	(17.7)	12,737	(70.0)	2,249	(12.4)	
50-59	5,106	(19.3)	17,543	(66.4)	3,774	(14.3)	
60-69	6,351	(23.6)	16,718	(62.1)	3,864	(14.4)	
70-79	2,831	(26.4)	6,390	(59.7)	1,489	(13.9)	
80+	317	(27.3)	675	(58.1)	170	(14.6)	
Race/ethnicity							
Non-Hispanic White	13,403	(20.9)	41,912	(65.4)	8,754	(13.7)	<0.01
Non-Hispanic Black	1,410	(21.0)	4,118	(61.3)	1,191	(17.7)	
American Indian / Alaskan Native	64	(18.2)	226	(64.4)	61	(17.4)	
Asian / Pacific Islander	1,525	(21.9)	4,408	(63.4)	1,017	(14.6)	
Hispanic	1,731	(21.8)	5,120	(64.5)	1,093	(13.8)	
Year of breast cancer diagnosis							
2004-2007	1,415	(14.7)	6,563	(68.3)	1,634	(17.0)	<0.01
2008-2011	6,184	(19.3)	21,133	(65.8)	4,803	(15.0)	
2012-2015	10,615	(23.8)	28,354	(63.4)	5,729	(12.8)	
AJCC stage							
I	12,005	(21.2)	37,287	(65.9)	7,258	(12.8)	<0.01
II	6,010	(20.9)	18,068	(62.8)	4,699	(16.3)	
III	199	(18.0)	695	(63.0)	209	(19.0)	
Tumor size, cm							
<2	13,715	(21.4)	42,295	(66.0)	8,032	(12.5)	<0.01
2-5	4,151	(20.0)	12,725	(61.2)	3,904	(18.8)	
>5	347	(21.6)	1,029	(64.1)	230	(14.3)	
Number positive axillary nodes							
0	15,524	(21.0)	47,945	(64.8)	10,533	(14.2)	<0.01
1-3	2,599	(21.9)	7,756	(65.4)	1,504	(12.7)	
4-9	66	(15.9)	257	(61.8)	93	(22.4)	
10+	25	(16.5)	92	(60.5)	35	(23.0)	
Grade							
1	6,667	(27.0)	17,002	(68.9)	1,018	(4.1)	<0.01
2	9,897	(21.4)	30,979	(67.1)	5,314	(11.5)	
3	1,208	(8.9)	6,706	(49.6)	5,607	(41.5)	
Unknown	426		1,312		181		
Progesterone receptor status							
Negative	264	(3.4)	4,376	(55.9)	3,191	(40.8)	<0.01
Positive	17,920	(22.8)	51,572	(65.7)	8,952	(11.4)	
Unknown	30		102		23		
Surgery							
None	106	(21.4)	306	(61.7)	84	(16.9)	<0.01
Breast-conserving surgery	12,193	(20.5)	39,122	(65.7)	8,227	(13.8)	
Mastectomy	5,901	(22.4)	16,576	(63.0)	3,842	(14.6)	
Unknown	14		46		13		
Radiation							
None	6,989	(21.6)	20,332	(63.0)	4,974	(15.4)	<0.01
Any	10,931	(20.9)	34,626	(66.2)	6,760	(12.9)	
Unknown	294		1,092		432		
Chemotherapy							
No/unknown	17,340	(25.7)	45,975	(68.1)	4,155	(6.2)	<0.01
Any	874	(4.6)	10,075	(53.1)	8,011	(42.3)	

eTable 2. Treatment of node-negative participants

	Non-Hispanic White (n=54,945)		Non-Hispanic Black (n=5,967)		American Indian / Alaskan Native (n=295)		Asian / Pacific Islander (n=6,034)		Hispanic (n=6,688)		P
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	
All women											
Surgery											
None	267	(0.5)	40	(0.7)	2	(0.7)	34	(0.6)	58	(0.9)	<0.01
Breast-conserving	39,179	(71.3)	4,014	(67.3)	193	(65.4)	3,882	(64.3)	4,631	(69.2)	
Mastectomy	15,450	(28.1)	1,638	(27.5)	100	(33.9)	2,114	(35.0)	1,994	(29.8)	
Radiation											
None	19,824	(36.1)	2,120	(35.5)	125	(42.4)	2,597	(43.0)	2,782	(41.6)	<0.01
Any	34,182	(62.2)	3,442	(57.7)	167	(56.6)	3,332	(55.2)	3,721	(55.6)	
Unknown	939	(1.7)	135	(2.3)	3	(1.0)	105	(1.7)	185	(2.8)	
Chemotherapy											
None/unknown	44,433	(80.9)	4,418	(74.0)	230	(78.0)	4,775	(79.1)	5,330	(79.7)	<0.01
Any	10,512	(19.1)	1,279	(21.4)	65	(22.0)	1,259	(20.9)	1,358	(20.3)	
RS 0-10											
Surgery											
None	53	(0.5)	12	(1.0)	2	(3.4)	7	(0.5)	13	(0.9)	<0.01
Breast-conserving	7,984	(69.7)	812	(68.1)	37	(62.7)	819	(62.1)	951	(66.3)	
Mastectomy	3,406	(29.7)	367	(30.8)	20	(33.9)	491	(37.3)	469	(32.7)	
Radiation											
None	4,209	(36.8)	479	(40.2)	27	(45.8)	594	(45.1)	601	(41.9)	<0.01
Any	7,102	(62.0)	690	(57.9)	32	(54.2)	710	(53.9)	796	(55.5)	
Unknown	142	(1.2)	23	(1.9)	0	(0.0)	14	(1.1)	37	(2.6)	
Chemotherapy											
None/unknown	11,191	(97.7)	1,153	(96.7)	57	(96.6)	1,278	(97.0)	1,385	(96.6)	0.04
Any	262	(2.3)	39	(3.3)	2	(3.4)	40	(3.0)	49	(3.4)	
RS 11-25											
Surgery											
None	180	(0.5)	18	(0.5)	0	(0.0)	21	(0.5)	38	(0.9)	<0.01
Breast-conserving	25861	(72.1)	2490	(71.2)	127	(68.6)	2511	(65.6)	3022	(70.0)	
Mastectomy	9816	(27.4)	987	(28.2)	58	(31.4)	1295	(33.8)	1251	(29.0)	
Radiation											
None	12601	(35.1)	1227	(35.1)	70	(37.8)	1598	(41.7)	1755	(40.7)	<0.01
Any	22730	(63.3)	2199	(62.9)	113	(61.1)	2168	(56.6)	2452	(56.8)	
Unknown	555	(1.5)	72	(2.1)	2	(1.1)	64	(1.7)	108	(2.5)	
Chemotherapy											
None/unknown	30543	(85.1)	2915	(83.3)	156	(84.3)	3185	(83.2)	3603	(83.5)	<0.01
Any	5343	(14.9)	583	(16.7)	29	(15.7)	645	(16.8)	712	(16.5)	
RS >25											
Surgery											
None	34	(0.4)	10	(1.0)	0	(0.0)	6	(0.7)	7	(0.7)	<0.01
Breast-conserving	5334	(70.1)	712	(70.7)	29	(56.9)	552	(62.3)	658	(70.1)	
Mastectomy	2228	(29.3)	284	(28.2)	22	(43.1)	328	(37.0)	274	(29.2)	
Radiation											
None	3014	(39.6)	414	(41.1)	28	(54.9)	405	(45.7)	426	(45.4)	<0.01
Any	4350	(57.2)	553	(54.9)	22	(43.1)	454	(51.2)	473	(50.4)	
Unknown	242	(3.2)	40	(4.0)	1	(2.0)	27	(3.0)	40	(4.3)	
Chemotherapy											
None/unknown	2699	(35.5)	350	(34.8)	17	(33.3)	312	(35.2)	342	(36.4)	0.22
Any	4907	(64.5)	657	(65.2)	34	(66.7)	574	(64.8)	597	(63.6)	

Abbreviations: RS, Recurrence Score

*To compare differences between groups we used chi-squared test (Fisher's exact test with cell frequencies <5)

eTable 3. Sensitivity Analysis: Risk of breast cancer-specific mortality according to the Recurrence Score and race/ethnicity restricted to node-negative tumors that are ER-positive and HER2-negative^a

	N	Breast cancer deaths	Age-adjusted model		Multivariable model ^b	
			SHR	(95% CI)	SHR	(95% CI)
All women, node-negative						
Non-Hispanic white	37,562	303	1.00	Reference	1.00	Reference
Non-Hispanic black	4,141	58	1.93	(1.46, 2.56)	1.72	(1.29, 2.31)
American Indian / Alaskan Native	226	3	1.82	(0.58, 5.67)	1.69	(0.54, 5.27)
Asian / Pacific Islander	4,404	15	0.52	(0.31, 0.88)	0.48	(0.29, 0.82)
Hispanic	5,003	32	0.99	(0.69, 1.43)	0.92	(0.64, 1.34)
Recurrence Score 0-10, node-negative						
Non-Hispanic white	8,483	32	1.00	Reference	1.00	Reference
Non-Hispanic black	909	9	2.75	(1.31, 5.77)	3.04	(1.43, 6.48)
American Indian / Alaskan Native	46	1	7.77	(1.06, 56.94)	8.96	(1.22, 65.99)
Asian / Pacific Islander	1,041	0	-	-	-	-
Hispanic	1,150	4	1.36	(0.48, 3.87)	1.11	(0.33, 3.69)
Recurrence Score 11-25, node-negative						
Non-Hispanic white	24,213	139	1.00	Reference	1.00	Reference
Non-Hispanic black	2,546	25	1.90	(1.24, 2.92)	1.62	(1.03, 2.56)
American Indian / Alaskan Native	143	2	2.69	(0.67, 10.88)	2.81	(0.69, 11.38)
Asian / Pacific Islander	2,752	5	0.42	(0.17, 1.04)	0.40	(0.16, 0.98)
Hispanic	3,195	13	0.89	(0.50, 1.57)	0.83	(0.47, 1.46)
Recurrence Score >25, node-negative						
Non-Hispanic white	4,866	132	1.00	Reference	1.00	Reference
Non-Hispanic black	686	24	1.47	(0.95, 2.28)	1.44	(0.92, 2.26)
American Indian / Alaskan Native	37	0	-	-	-	-
Asian / Pacific Islander	611	10	0.63	(0.33, 1.20)	0.58	(0.30, 1.10)
Hispanic	658	15	1.01	(0.59, 1.73)	0.99	(0.58, 1.69)

Abbreviations: SHR, subdistribution hazard ratio.

^aRestricted to cases diagnosed between 2010-2015.

^bMultivariable Fine-Gray model with robust standard errors adjusted for age, year of diagnosis, tumor size, progesterone receptor status, type of surgery, and administration of radiation and chemotherapy.

eTable 4. Risk of breast cancer-specific mortality among node-positive patients, according to the Recurrence Score and race/ethnicity

	N	Breast cancer deaths	Age-adjusted model		Multivariable-adjusted model ^a	
			SHR	(95% CI)	SHR	(95% CI)
All node-positive						
Non-Hispanic White	9,124	220	1.00	Reference	1.00	Reference
Non-Hispanic Black	1,022	32	1.60	(1.10, 2.32)	1.31	(0.88, 1.93)
American Indian / Alaskan Native	56	2	1.65	(0.41, 6.66)	1.61	(0.40, 6.51)
Asian / Pacific Islander	916	13	0.84	(0.48, 1.47)	0.84	(0.54, 0.91)
Hispanic	1,256	27	1.19	(0.80, 1.78)	1.11	(0.74, 1.68)
Recurrence Score 0-10						
Non-Hispanic White	1,950	22	1.00	Reference	1.00	Reference
Non-Hispanic Black	218	1	0.54	(0.07, 4.03)	0.43	(0.06, 3.30)
American Indian / Alaskan Native	5	0	-	-	-	-
Asian / Pacific Islander	207	0	-	-	-	-
Hispanic	297	2	0.80	(0.19, 1.12)	0.76	(0.18, 3.25)
Recurrence Score 11-25						
Non-Hispanic White	6,026	104	1.00	Reference	1.00	Reference
Non-Hispanic Black	620	17	1.95	(1.17, 3.26)	1.96	(1.16, 3.30)
American Indian / Alaskan Native	41	2	2.95	(0.73, 11.98)	3.07	(0.75, 12.52)
Asian / Pacific Islander	578	6	0.93	(0.41, 2.12)	0.93	(0.41, 2.14)
Hispanic	805	13	1.28	(0.72, 2.29)	1.21	(0.67, 2.15)
Recurrence Score >25						
Non-Hispanic White	1,148	94	1.00	Reference	1.00	Reference
Non-Hispanic Black	184	14	1.17	(0.67, 2.05)	0.89	(0.48, 1.68)
American Indian / Alaskan Native	10	0	-	-	-	-
Asian / Pacific Islander	131	7	0.91	(0.42, 1.97)	0.85	(0.39, 1.87)
Hispanic	154	12	1.36	(0.74, 2.49)	1.30	(0.69, 2.46)

Abbreviations: SHR, subdistribution hazard ratio.

^aMultivariable Fine-Gray model with robust standard errors adjusted for age, year of diagnosis, tumor size, progesterone receptor status, type of surgery, and administration of radiation and chemotherapy.

eTable 5. Performance of the Recurrence Score in axillary lymph node-negative patients, by race/ethnicity

	N	Breast cancer deaths	Age-adjusted model		Multivariable model ^a		C-index ^b (95% CI)	
			SHR	(95% CI)	SHR	(95% CI)		
All women, node-negative								
RS								
0-10	15,524	90	1.00	Reference	1.00	Reference	0.660	(0.642, 0.678)
11-25	47,945	516	1.70	(1.35, 2.12)	1.78	(1.43, 2.16)		
>25	10,533	430	6.09	(4.85, 7.64)	5.76	(4.46, 7.44)		
<i>Per 10-unit increase in the RS</i>			1.82	(1.73, 1.91)	1.73	(1.63, 1.83)	0.697	(0.677, 0.717)
Non-Hispanic White								
RS								
0-10	11,453	65	1.00	Reference	1.00	Reference	0.660	(0.640, 0.681)
11-25	35,886	402	1.81	(1.39, 2.35)	1.87	(1.42, 2.46)		
>25	7,606	315	6.29	(4.82, 8.35)	5.79	(4.29, 7.82)		
<i>Per 10-unit increase in the RS</i>			1.80	(1.70, 1.91)	1.71	(1.60, 1.83)	0.700	(0.677, 0.722)
Non-Hispanic Black								
RS								
0-10	1,192	15	1.00	Reference	1.00	Reference	0.627	(0.573, 0.682); P< 0.001 ^c
11-25	3,498	58	1.22	(0.69, 2.17)	1.24	(0.69, 2.23)	Diff: -0.033	(-0.067, 0.001)
>25	1,007	53	3.94	(2.21, 7.00)	3.48	(1.83, 6.63)		
<i>Per 10-unit increase in the RS</i>			1.63	(1.43, 1.85)	1.58	(1.35, 1.84)	0.656	(0.592, 0.720); P < 0.01 ^c Diff: -0.044 (-0.085, -0.002)
American Indian / Alaskan Native								
RS								
0-10	59	1	1.00	Reference	1.00	Reference	0.576	(0.321, 0.831); P<0.01 ^c
11-25	185	2	0.66	(0.06, 7.29)	0.30	(0.02, 4.46)	Diff: -0.084	(-0.319, 0.150)
>25	51	2	2.21	(0.20, 24.52)	0.37	(0.02, 7.00)		
<i>Per 10-unit increase in the RS</i>			2.36	(1.31, 4.27)	1.74	(0.74, 4.11)	0.701	(0.429, 0.975); P=0.968 ^c Diff: 0.001 (-0.248, 0.253)
Asian / Pacific Islander								
RS								
0-10	1,318	1	1.00	Reference	1.00	Reference	0.740	(0.675, 0.806); P<0.001 ^c
11-25	3,830	23	7.05	(0.95, 52.32)	0.42	(0.04, 4.92)	Diff: 0.080	(0.035, 0.125)
>25	885	26	29.90	(4.06, 220.5)	2.66	(0.21, 34.19)		
<i>Per 10-unit increase in the RS</i>			2.10	(1.69, 2.60)	2.04	(1.61, 2.59)	0.784	(0.720, 0.847); P<0.001 ^c Diff: 0.084 (0.043, 0.125)
Hispanic								
RS								
0-10	1,434	8	1.00	Reference	1.00	Reference	0.667	(0.597, 0.737); P=0.254 ^c
11-25	4,315	31	1.19	(0.54, 2.58)	-	-	Diff: 0.007	(-0.043, 0.056)
>25	939	34	5.58	(2.58, 12.07)	-	-		
<i>Per 10-unit increase in the RS</i>			2.03	(1.69, 2.43)	2.29	(1.85, 2.84)	0.678	(0.594, 0.761); P<0.001 ^c Diff: -0.022 (-0.083, 0.039)

Abbreviations: RS, Recurrence Score; SHR, subdistribution hazard ratio; Diff, difference in the C-index between indicated racial/ethnic group and non-Hispanic White.

^aMultivariable Fine-Gray model with robust standard errors adjusted for age, year of diagnosis, tumor size, progesterone receptor status, type of surgery, and administration of radiation and chemotherapy.

^bC-index estimated from rank parameter Harrell's C with symmetric 95% confidence intervals for the crude hazard ratio.

^cPairwise comparisons of C-indexes¹ were performed with a reference group of non-Hispanic white.

eReference

1. Kang L, Chen W, Petrick NA, Gallas BD. Comparing two correlated C indices with right-censored survival outcome: a one-shot nonparametric approach. *Statistics in medicine*. 2015;34(4):685-703.