Supplemental Materials

Menstrual and reproductive characteristics and breast cancer risk by hormone receptor status and race/ethnicity: The Breast Cancer Etiology in Minorities (BEM) Study

Esther M. John, Amanda I. Phipps, Lisa M. Hines, Jocelyn Koo, Sue A. Ingles, Kathy B. Baumgartner, Martha L. Slattery, Anna H. Wu

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Supplemental Methods

The Breast Cancer Etiology in Minorities (BEM) study harmonized interview data from four population-based studies of breast cancer, as described elsewhere.[1]

The San Francisco Bay Area Breast Cancer Study (SFBCS) is a population-based case-control study conducted in Hispanic, African American, and non-Hispanic white (NHW) women aged 35-79 years from the San Francisco Bay Area.[2] Cases were women diagnosed with a first primary invasive breast cancer from 1995-2002. Newly diagnosed cases were identified through the Greater Bay Area Cancer Registry and screened by telephone to assess self-identified race/ethnicity and study eligibility. Of those contacted, 89% completed the screening interview, and of cases invited to participate in the study (all Hispanic cases diagnosed from 1995-2002, all African American cases diagnosed from 1995-1999, and a 10% random sample of NHW cases diagnosed from 1995-1999), 2,256 (88%) completed an in-person interview, including 1,118 Hispanics, 543 African Americans, and 595 NHWs. Random-digit dialing was used to identify controls aged 35-79 years. They were frequency-matched to cases on race/ethnicity and the expected 5-year age distribution of cases at a ratio of 1 control per case, except for Hispanics diagnosed from 1995-1998 for whom a ratio of 1.5 controls per case was used. Participation in the screening interview was 92%, and of 3,170 eligible controls without a personal history of breast cancer, 2,706 (85%) completed the in-person interview, including 1,462 Hispanics, 598 African Americans, and 646 NHWs.

The Northern California Breast Cancer Family Registry (NC-BCFR) is a population-based family study that also included a set of population controls. Women aged 18-64 years with newly diagnosed breast cancer were identified through the Greater Bay Area Cancer Registry (diagnoses 1995-2009) and the Sacramento and Sierra cancer registries (diagnoses 2005-2006).[3] All cases with any indicators of increased genetic susceptibility (i.e., diagnosis at ages 18-34 years, a personal history of breast ovarian or childhood cancer, bilateral breast cancer with a first diagnosis before age 50 years, or a first-degree family history of breast, ovarian or childhood cancer) were eligible to enroll in the NC-BCFR. Cases who did not meet any of these criteria, were randomly sampled (2.5% of NHWs and 50% of other race/ethnicity groups). Study eligibility was determined based on cancer registry data or a telephone screening interview that assessed self-identified race/ethnicity and personal and family history of breast, ovarian or childhood cancer. Of cases contacted, 85% completed the screening interview, and of those selected, 3,620 (76%) enrolled in the NC-BCFR and completed questionnaires on cancer family history and other breast cancer risk factors. Minorities accounted for 75% of enrolled cases. For the present analysis, we restricted cases to those diagnosed with a first primary invasive breast cancer between 1995 and 2003, and we excluded 325 cases who also participated in the SFBCS, leaving 1,893 cases (290 Hispanics, 308 African Americans, 727 Asian Americans (346 Chinese, 241 Filipinas, 80 Japanese, 60 other Asians or other race/ethnicity), and 568 NHWs for analysis. Random-digit dialing was used to identify controls aged 18-64 years. They were frequency-matched to cases diagnosed from 1995-1998 on race/ethnicity and 5-year age group, at a ratio of 1 control per 2 cases. Participation in the screening interview was 82%, and of eligible controls without a personal history of breast cancer, 626 (91%) completed the in-person interview, including 387 NHWs, 74 Chinese, Japanese or Filipinas, 73 Hispanics, 73 African Americans, and 19 other Asians or other race/ethnicity.

The 4-Corners Breast Cancer Study (4-CBCS) is a population-based case-control study conducted in Hispanic, Native American, and NHW women aged 25-79 years from non-reservation areas of Arizona, Colorado, New Mexico, and Utah.[4] Cases newly diagnosed with breast cancer from 1999-2004 were identified through the state cancer registries. Of cases

contacted, 2,556 (68%) completed the in-person interview. For the present analysis, we restricted cases to those with a first primary invasive breast cancer, including 1,928 cases (667 Hispanics/Native Americans and 1,261 NHWs). Controls aged 36-79 years were selected from the populations living in the four states. They were frequency-matched to cases on race/ethnicity and expected 5-year age distribution. Of controls contacted, 2,524 (41%) without a personal history of breast cancer completed the in-person interview, including 924 Hispanics/Native Americans and 1,600 NHWs.

The Los Angeles County Asian American Breast Cancer Study is a population-based case-control study in Chinese, Japanese and Filipina women aged 25-74 years from Los Angeles County.[5] Women newly diagnosed with breast cancer from 1995-2001 or from 2003-2006 were identified through the Los Angeles County Cancer Surveillance Program. Of those contacted, 2,303 (73%) completed the in-person interview. The present analysis was restricted to 1,818 cases with invasive breast cancer, including 746 Chinese, 428 Japanese, and 644 Filipinas. Block walking in the neighborhoods where the cases were diagnosed was used to identify controls aged 25-74 years. They were frequency-matched to cases on specific Asian ethnicity and 5-year age group. In-person interviews were completed for 1,911 controls without a personal history of breast cancer, including 869 Chinese, 492 Japanese, and 550 Filipinas.

Pooled dataset. The pooled dataset included 5,467 cases with hormone receptor positive breast cancer, 1,435 cases with hormone receptor negative breast cancer, and 7,767 controls without a personal history of breast cancer. Study exclusions are shown in Supplemental Figure 1.

References

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Supplemental Table 1 Menstrual and reproductive characteristics and risk of breast cancer by hormone receptor status, race/ethnicity, and age

	Non-Hispanic white				African American				Hispanic				Asian Americans			
	Cs	Cn	OR	95% CI [a]	Cs	Cn	OR	95% CI [a]	Cs	Cn	OR	95% CI [a]	Cs	Cn	OR	95% CI [a]
Age at menarche [b]																
Women ages <50 years																
HR+ breast cancer																
<12	103	161	1.0		40	59	1.0		151	217	1.0		172	172	1.0	
12	162	247	0.97	0.64-1.46	56	67	1.59	0.83-3.04	148	217	0.88	0.63-1.24	223	278	0.85	0.63-1.15
13	150	249	0.90	0.59-1.37	51	54	1.30	0.66-2.54	126	219	0.72	0.51-1.01	191	266	0.69	0.50-0.94
≥14	134	230	0.79	0.52-1.22	45	46	1.61	0.80-3.22	119	276	0.58	0.41-0.83	220	282	0.76	0.55-1.04
P trend				0.25				0.32				<0.01				0.047
P heterogeneity by race/ethnicity = 0.56																
HR- breast cancer																
<12	32	161	1.0		27	59	1.0		61	217	1.0		43	172	1.0	
12	56	247	0.89	0.47-1.68	29	67	0.92	0.44-1.92	51	217	0.66	0.41-1.05	50	278	0.78	0.47-1.29
13	53	249	1.04	0.55-1.96	18	54	0.47	0.20-1.09	60	219	0.80	0.50-1.28	47	266	0.70	0.42-1.17
≥14	23	230	0.56	0.27-1.13	20	46	0.66	0.29-1.53	53	276	0.61	0.38-0.97	41	282	0.61	0.37-1.03
P trend				0.18				0.14				0.08				0.07
P heterogeneity by race/ethnicity = 0.71																
P heterogeneity by subtype				0.22				0.14				0.51				0.37
Women ages ≥50 years																
HR+ breast cancer																
<12	230	314	1.0		80	90	1.0		188	288	1.0		160	166	1.0	
12	287	438	0.88	0.67-1.16	79	101	1.10	0.68-1.79	196	297	0.97	0.73-1.30	225	242	1.06	0.78-1.45
13	318	446	0.95	0.73-1.24	78	120	0.82	0.51-1.33	172	351	0.74	0.56-0.99	252	231	1.19	0.87-1.62
≥14	260	458	0.74	0.56-0.97	107	126	1.12	0.70-1.77	222	471	0.77	0.58-1.01	359	336	1.39	1.03-1.87
P trend				0.05				0.89				0.02				0.01
P heterogeneity by race/ethnicity = 0.06																
HR- breast cancer																
<12	40	314	1.0		33	90	1.0		54	288	1.0		27	166	1.0	
12	47	438	0.79	0.48-1.29	32	101	1.38	0.73-2.64	40	297	0.69	0.43-1.09	58	242	1.55	0.90-2.68
13	45	446	0.71	0.43-1.19	31	120	0.83	0.42-1.62	43	351	0.60	0.38-0.94	57	231	1.63	0.94-2.82
≥14	40	458	0.62	0.37-1.04	26	126	0.61	0.31-1.23	56	471	0.66	0.43-1.02	97	336	1.98	1.17-3.34
P trend				0.07				0.06				0.06				0.01

P heterogeneity by race/ethnicity < 0.01																
P heterogeneity by subtype				0.53				0.12				0.75				0.31
HR+ subtype: P heterogeneity by age				0.49				0.27				0.51				0.03
HR- subtype: P heterogeneity by age				0.99				0.95				0.56				<0.01
Nulliparity																
HR+ breast cancer																
Women ages <50 years																
Parous	374	659	1.0		152	186	1.0		446	842	1.0		551	789	1.0	
Nulliparous	175	228	1.30	0.94-1.80	40	40	0.99	0.54-1.82	98	87	1.66	1.15-2.39	255	209	1.88	1.48-2.39
P heterogeneity by race/ethnicity <0.01																
Women ages ≥50 years																
Parous	924	1436	1.0		279	390	1.0		702	1318	1.0		776	844	1.0	
Nulliparous	171	220	1.18	0.90-1.54	65	47	1.92	1.21-3.04	76	89	1.59	1.11-2.29	220	131	1.89	1.46-2.43
P heterogeneity by race/ethnicity <0.01																
HR+ subtype: P heterogeneity by age				0.9				0.12				0.99				0.65
Age at first FTP (years), parous women [b]																
HR+ breast cancer																
Women ages <50 years																
< 20	42	70	1.0		58	72	1.0		100	268	1.0		18	34	1.0	
20-24	102	221	0.88	0.50-1.56	51	62	0.96	0.51-1.83	154	289	1.34	0.94-1.89	88	157	1.28	0.63-2.61
25-29	118	190	1.09	0.60-1.97	27	30	1.49	0.67-3.31	109	184	1.40	0.94-2.07	214	313	1.55	0.77-3.11
≥30	112	178	0.91	0.47-1.75	16	22	0.79	0.30-2.11	83	101	1.75	1.09-2.82	231	285	1.78	0.88-3.61
P trend				0.98				0.9				0.02				0.04
P heterogeneity by race/ethnicity <0.01																
Women ages ≥50 years																
< 20	136	223	1.0		116	174	1.0		179	376	1.0		45	57	1.0	
20-24	415	665	1.17	0.86-1.58	101	150	1.09	0.72-1.66	286	560	1.06	0.82-1.37	217	269	0.80	0.50-1.28
25-29	254	381	1.01	0.72-1.42	34	46	0.91	0.49-1.69	140	261	0.97	0.71-1.33	335	337	0.97	0.60-1.57
≥30	119	167	1.12	0.74-1.71	28	20	2.72	1.27-5.80	97	121	1.16	0.79-1.72	179	181	0.83	0.49-1.41
P trend				0.99				0.08				0.68				0.99
P heterogeneity by race/ethnicity = 0.08																
HR+ subtype: P heterogeneity by age				0.90				0.39				0.07				0.26
Interval between menarche and first FTP (years), parous women [c]																
HR+ breast cancer																

Women ages <50 years																
<8	53	96	1.0		67	80	1.0		118	321	1.0		28	58	1.0	
8-10	58	145	0.76	0.42-1.36	28	42	0.82	0.40-1.66	103	172	1.42	0.97-2.06	52	94	1.34	0.72-2.51
11-14	96	152	1.26	0.72-2.21	31	27	1.32	0.61-2.87	92	179	1.15	0.78-1.70	139	205	1.45	0.82-2.58
≥15	167	266	0.94	0.53-1.69	26	37	1.12	0.50-2.52	133	170	1.73	1.15-2.59	332	432	1.61	0.91-2.86
P trend				0.72				0.62				0.03				0.10
P heterogeneity by race/ethnicity = 0.01																
Women ages ≥50 years																
<8	186	354	1.0		141	208	1.0		224	507	1.0		82	121	1.0	
8-10	246	377	1.24	0.92-1.66	60	85	1.07	0.66-1.71	185	329	1.17	0.89-1.54	153	149	1.24	0.83-1.86
11-14	267	411	1.09	0.81-1.48	37	62	0.95	0.54-1.67	153	274	0.97	0.72-1.31	242	276	1.10	0.74-1.62
≥15	225	294	1.28	0.91-1.81	41	35	1.69	0.91-3.13	140	208	0.96	0.69-1.35	299	298	1.21	0.80-1.84
P trend				0.29				0.22				0.68				0.55
P heterogeneity by race/ethnicity = 0.71																
HR+ subtype: P heterogeneity by age				0.63				0.53				0.02				0.31
Time since last FTP (years), parous women [b]																
Women ages <50 years																
HR+ breast cancer																
≥20	62	113	1.0		44	68	1.0		91	130	1.0		56	77	1.0	
10-19	174	285	1.44	0.88-2.34	64	78	1.25	0.64-2.45	191	416	0.96	0.66-1.40	268	369	1.33	0.86-2.05
3-9	92	187	1.22	0.66-2.25	33	29	1.36	0.49-3.76	127	232	1.49	0.94-2.35	176	273	1.56	0.95-2.57
<3	46	73	1.59	0.67-3.80	10	11	0.99	0.21-4.62	37	64	1.81	0.94-3.50	51	70	2.03	1.03-3.99
P trend				0.49				0.72				0.02				0.04
P heterogeneity by race/ethnicity = 0.76																
HR- breast cancer																
≥20	17	113	1.0		22	68	1.0		35	130	1.0		11	77	1.0	
10-19	46	285	0.99	0.45-2.15	33	78	1.11	0.49-2.52	77	416	0.97	0.57-1.64	58	369	1.20	0.56-2.57
3-9	29	187	0.56	0.21-1.55	17	29	1.56	0.50-4.80	66	232	1.63	0.85-3.10	58	273	1.62	0.69-3.80
<3	15	73	0.61	0.15-2.44	7	11	0.75	0.13-4.51	17	64	1.38	0.56-3.40	17	70	1.66	0.55-5.01
P trend				0.27				0.76				0.15				0.23
P heterogeneity by race/ethnicity =0.38																
P heterogeneity by subtype				0.63				0.40				0.57				0.39
Parity, parous women [c]																
Women ages <50 years																
HR+ breast cancer																
1	93	144	1.0		50	54	1.0		105	109	1.0		180	201	1.0	

2	186	291	1.18	0.79-1.78	46	73	0.62	0.33-1.18	163	267	0.68	0.46-0.99	256	387	0.76	0.57-1.01
3	62	128	0.73	0.43-1.25	32	35	1.02	0.47-2.24	106	243	0.50	0.33-0.77	89	149	0.67	0.46-0.99
≥4	33	96	0.73	0.41-1.31	24	24	1.07	0.45-2.53	72	223	0.47	0.29-0.76	26	52	0.67	0.37-1.22
P trend				0.12				0.69				<0.01				0.03
P heterogeneity by race/ethnicity = 0.06																
HR- breast cancer																
1	28	144	1.0		24	54	1.0		31	109	1.0		46	201	1.0	
2	47	291	0.91	0.47-1.77	26	73	0.84	0.40-1.79	72	267	0.78	0.45-1.35	59	387	0.57	0.36-0.92
3	26	128	0.97	0.43-2.16	20	35	1.83	0.73-4.59	55	243	0.66	0.36-1.19	30	149	0.72	0.40-1.32
≥4	8	96	0.54	0.19-1.53	9	24	0.70	0.21-2.33	37	223	0.67	0.34-1.31	9	52	0.68	0.27-1.72
P trend				0.35				0.85				0.21				0.26
P heterogeneity race/ethnicity = 0.27																
P heterogeneity subtype				0.65				0.79				0.10				0.30
Women ages ≥50 years																
HR+ breast cancer																
1	119	187	1.0		52	67	1.0		89	116	1.0		131	134	1.0	
2	380	482	1.21	0.87-1.68	83	88	1.35	0.78-2.36	180	230	1.09	0.75-1.59	325	289	1.07	0.78-1.47
3	213	383	0.88	0.61-1.25	63	95	1.16	0.66-2.04	161	318	0.74	0.50-1.09	179	209	0.83	0.58-1.19
≥4	212	384	0.88	0.61-1.27	81	140	1.17	0.67-2.06	272	654	0.66	0.45-0.96	141	212	0.62	0.42-0.91
P trend				0.07				0.83				<0.01				<0.01
P heterogeneity by race/ethnicity <0.01																
HR+ subtype: P heterogeneity by age				0.74				0.63				0.12				0.89
HR- breast cancer																
1	20	187	1.0		22	67	1.0		14	116	1.0		38	134	1.0	
2	56	482	1.02	0.55-1.89	33	88	0.65	0.32-1.34	46	230	1.45	0.75-2.81	83	289	0.97	0.60-1.57
3	49	383	1.08	0.56-2.08	27	95	0.59	0.28-1.25	35	318	0.95	0.48-1.90	47	209	0.66	0.38-1.14
≥4	29	384	0.68	0.33-1.38	27	140	0.54	0.26-1.11	83	654	1.07	0.55-2.08	34	212	0.49	0.27-0.91
P trend				0.23				0.11				0.59				<0.01
P heterogeneity by race/ethnicity = 0.04																
P heterogeneity subtype				0.88				0.15				0.13				0.38
HR+ subtype: P heterogeneity by age				0.74				0.63				0.12				0.89
HR- subtype: P heterogeneity by age				0.96				0.61				0.19				0.66
Lifetime breast-feeding (months), parous women [d]																
Women ages <50 years																
HR+ breast cancer																
0	75	102	1.0		72	99	1.0		136	190	1.0		237	381	1.0	

1-12	163	274	0.77	0.49-1.22	56	59	1.69	0.93-3.10	179	307	0.86	0.62-1.19	237	267	1.00	0.74-1.35
13-24	67	141	0.57	0.33-1.01	13	18	0.64	0.23-1.81	73	152	0.85	0.56-1.28	47	91	0.65	0.41-1.02
≥25	69	142	0.76	0.42-1.35	11	10	1.51	0.49-4.64	58	193	0.58	0.37-0.90	30	50	0.64	0.36-1.15
P trend				0.24				0.62				0.02				0.05
P heterogeneity by race/ethnicity = 0.29																
HR- breast cancer																
0	22	102	1.0		44	99	1.0		51	190	1.0		67	381	1.0	
1-12	41	274	0.68	0.32-1.41	29	59	1.00	0.48-2.07	87	307	0.95	0.61-1.48	58	267	0.74	0.45-1.21
≥13	46	283	1.30	0.60-2.84	6	28	0.39	0.13-1.16	57	345	0.74	0.45-1.22	19	141	0.42	0.21-0.83
P trend				0.36				0.16				0.23				0.01
P heterogeneity by race/ethnicity = 0.69																
P heterogeneity by subtype				0.09				<0.01				0.81				0.31
Women ages ≥50 years																
HR+ breast cancer																
0	367	518	1.0		164	209	1.0		296	456	1.0		385	418	1.0	
1-12	367	566	0.94	0.75-1.18	64	103	0.67	0.44-1.04	219	398	0.82	0.65-1.05	253	277	0.69	0.53-0.90
13-24	102	180	0.84	0.60-1.18	25	36	1.15	0.61-2.17	78	178	0.77	0.55-1.08	58	76	0.62	0.41-0.94
≥25	88	172	0.90	0.63-1.30	26	42	0.96	0.51-1.81	109	286	0.75	0.54-1.03	80	73	0.87	0.56-1.34
P trend				0.38				0.84				0.04				0.08
P heterogeneity by race/ethnicity = 0.10																
HR- breast cancer																
0	58	518	1.0		67	209	1.0		74	456	1.0		101	418	1.0	
1-12	69	566	1.14	0.75-1.74	23	103	0.88	0.49-1.59	53	398	0.77	0.51-1.14	72	277	0.74	0.49-1.12
≥13	27	352	0.89	0.51-1.55	19	78	1.11	0.56-2.20	51	464	0.66	0.43-1.03	29	149	0.53	0.30-0.92
P trend				0.82				0.90				0.06				0.02
P heterogeneity by race/ethnicity = 0.76																
P heterogeneity by subtype				0.73				0.99				0.59				0.18
HR+ subtype: P heterogeneity by age				0.92				0.56				0.15				0.34
HR- subtype: P heterogeneity by age				0.46				0.47				0.71				0.36

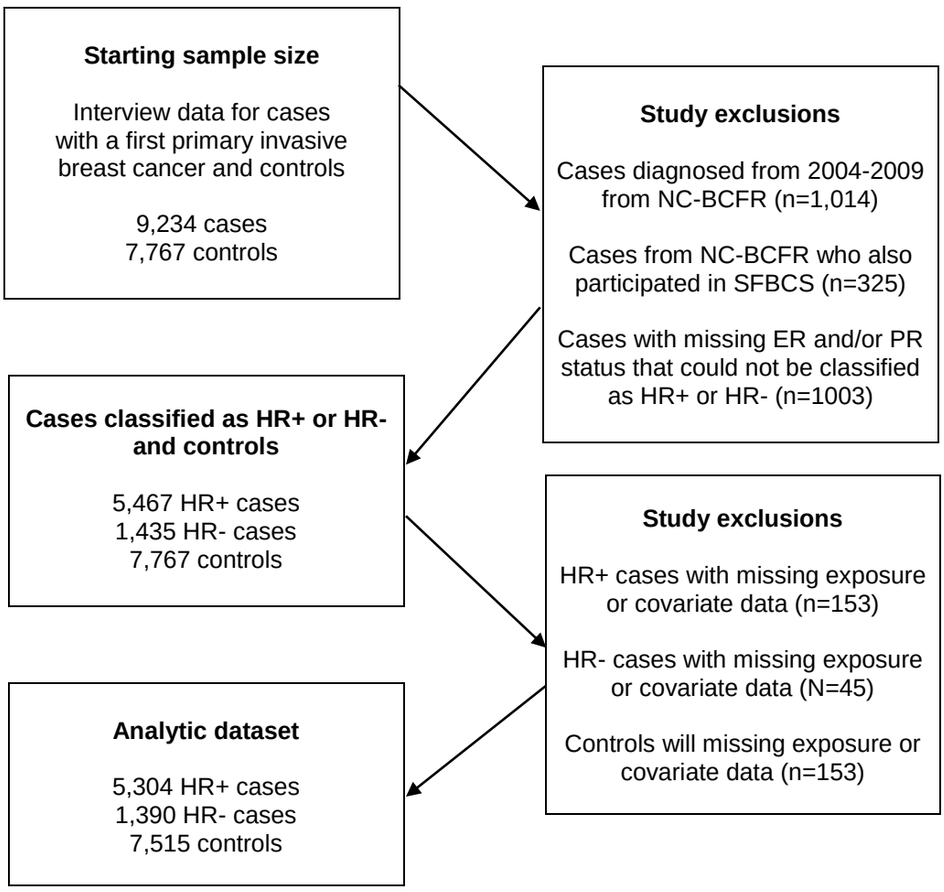
Abbreviations: BMI, body mass index; CI, confidence interval; Cs, cases; Cn, controls; ER, estrogen receptor; FTP, full-term pregnancy; HR+, hormone receptor positive (ER+ or PR+); HR-, hormone receptor negative (ER- and PR-); OR, odds ratio; PR, progesterone receptor.

Covariates were categorized as follows: Study (AABCS, NC-BCFR, SFBCS, 4-CBCS); year of diagnosis or selection/interview (1995-1998, 1999-2001, 2002-2007); race/ethnicity (non-Hispanic white, African American, Hispanic, Asian American); education (some high school or less, high school graduate, some college or vocational/technical school, college graduate or

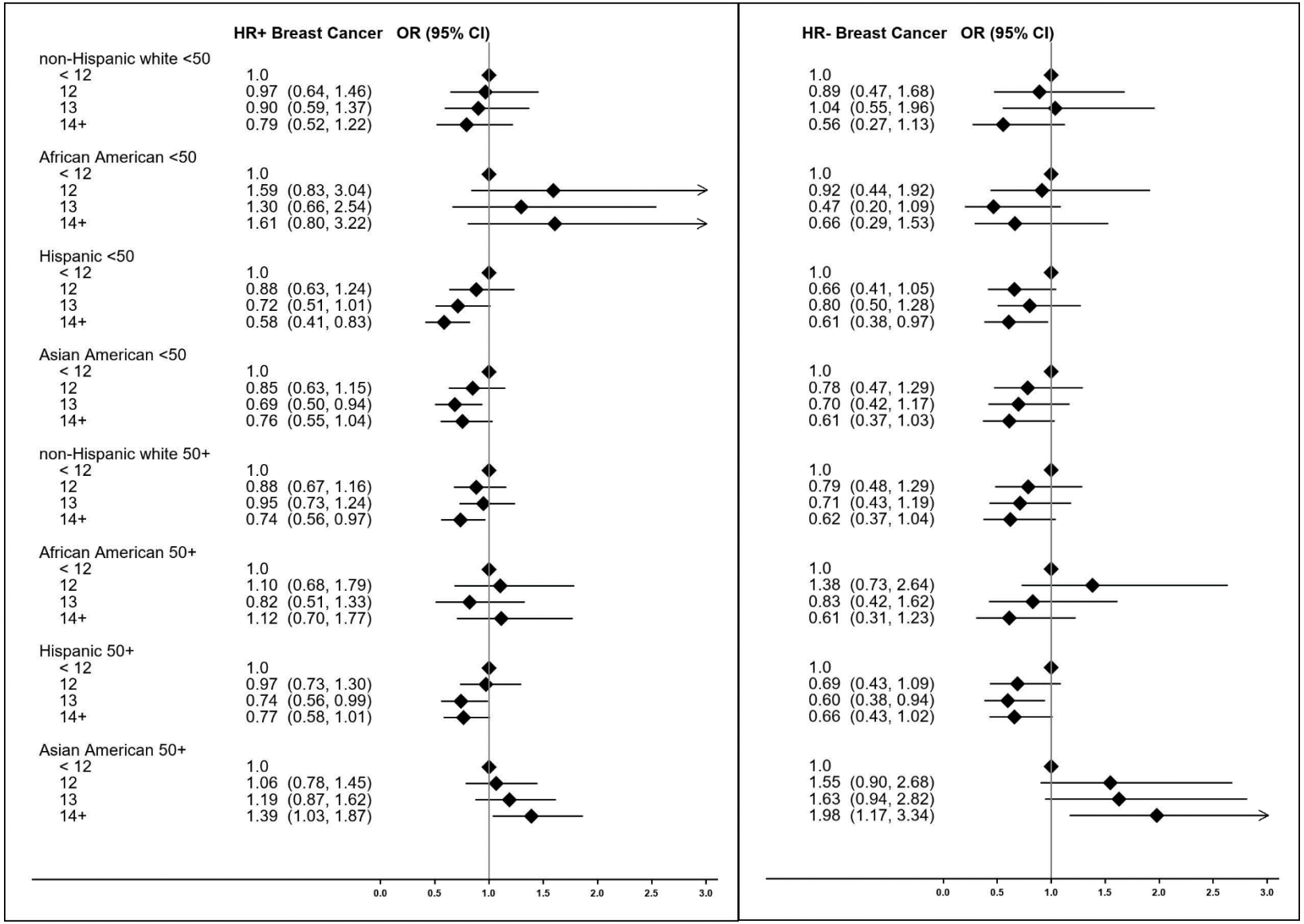
higher degree); first-degree family history of breast cancer (yes, no); personal history of benign breast disease (yes, no); alcohol consumption in reference year (none, <4, ≥5 drinks per week); BMI in reference year (<25.0, 25.0-29.9, ≥30.0 kg/m^2); age at menarche (<12, 12, 13, ≥14 years); age at first FTP (nulliparous, <20, 20-24, 25-29, ≥30 years); parity (nulliparous, 1, 2, 3, ≥4 FTPs); lifetime breast-feeding (nulliparous, 0, 1-12, 13-24, ≥25 months).

[a] Adjusted for age at diagnosis or selection/interview (continuous), study, year of diagnosis or selection/interview, education, first-degree family history of breast cancer, personal history of benign breast disease, age at menarche, alcohol consumption, and BMI.
[b] Additionally adjusted for parity and breast-feeding
[c] Additionally adjusted for age at first FTP and breast-feeding.
[d] Additionally adjusted for age at first FTP and parity.

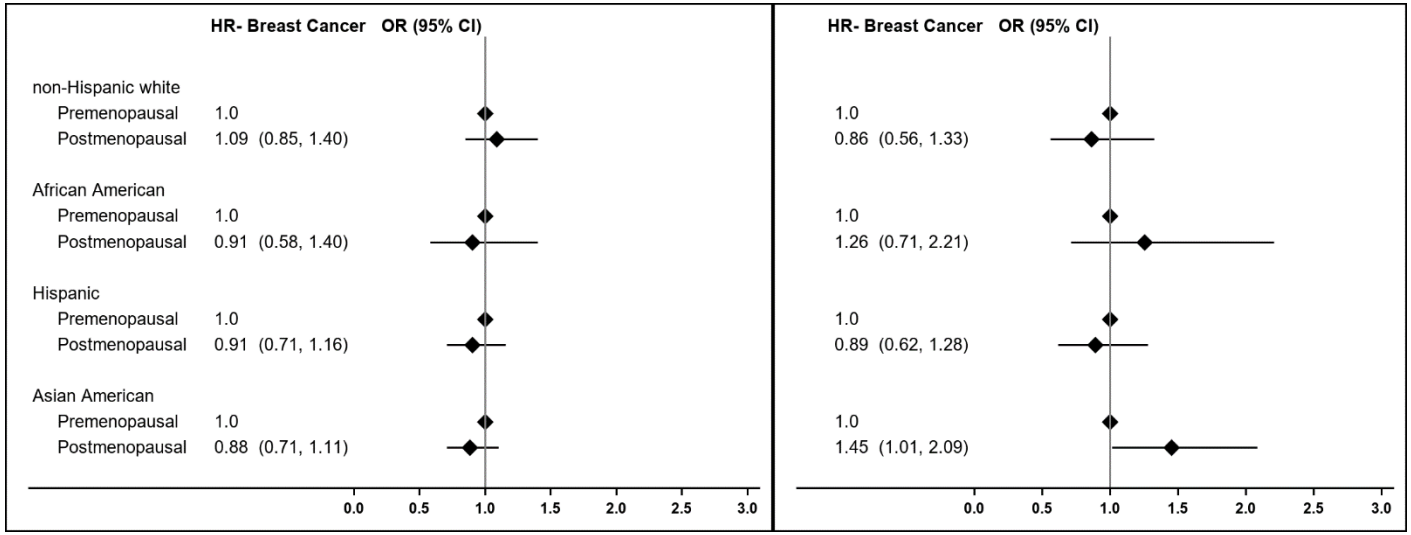
Supplemental Figure 1. Flow chart of study participants



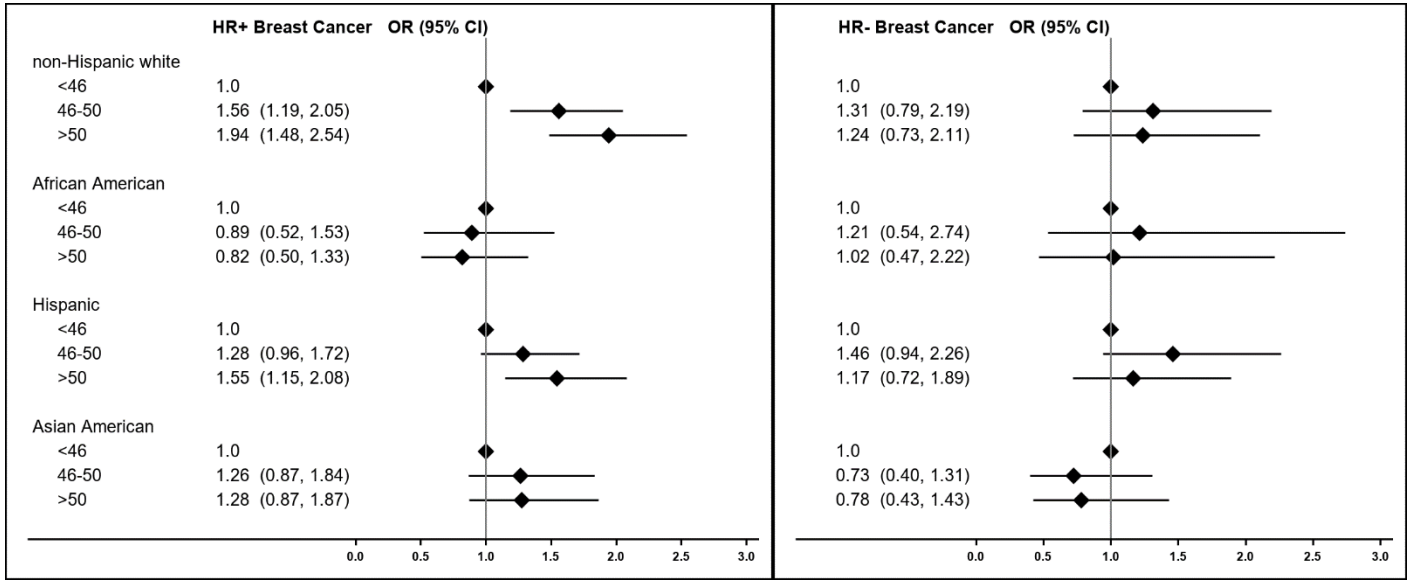
Supplemental Figure 2-A. Age at menarche and risk of breast cancer by hormone receptor status, race/ethnicity and age



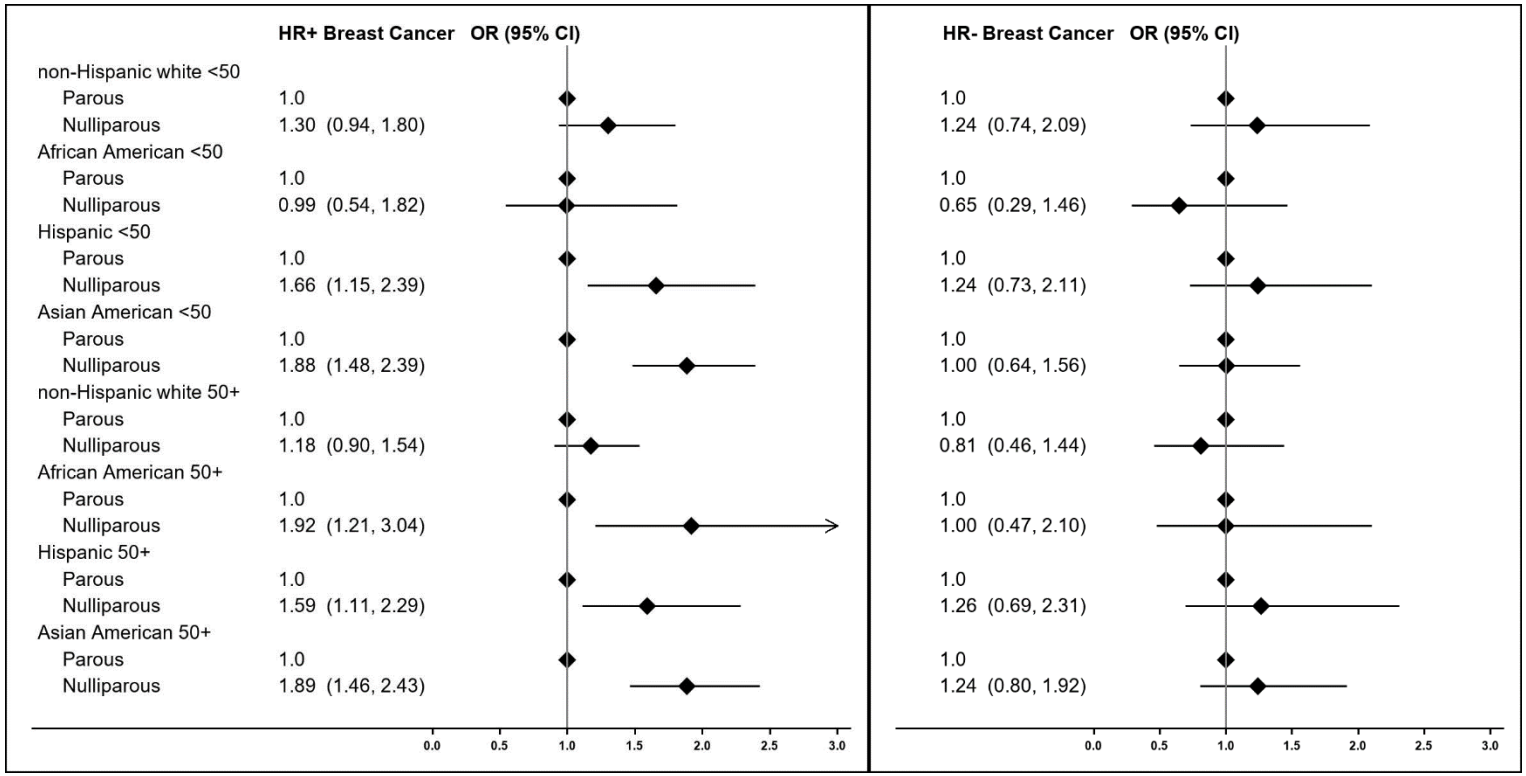
Supplemental Figure 2-B. Menopausal status and risk of breast cancer by hormone receptor status, race/ethnicity



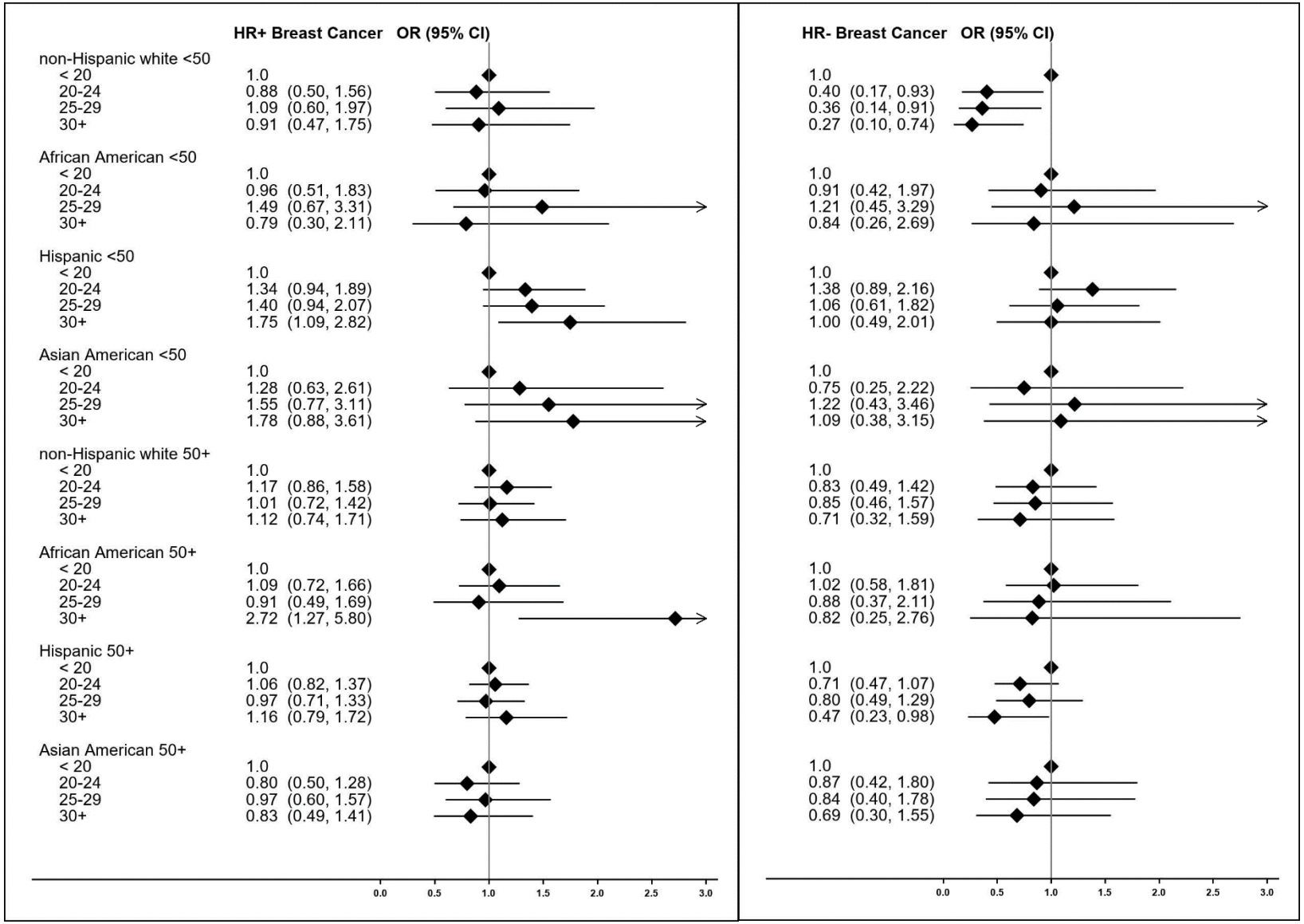
Supplemental Figure 2-C. Age at menopause and risk of breast cancer by hormone receptor status, race/ethnicity, women with natural menopause



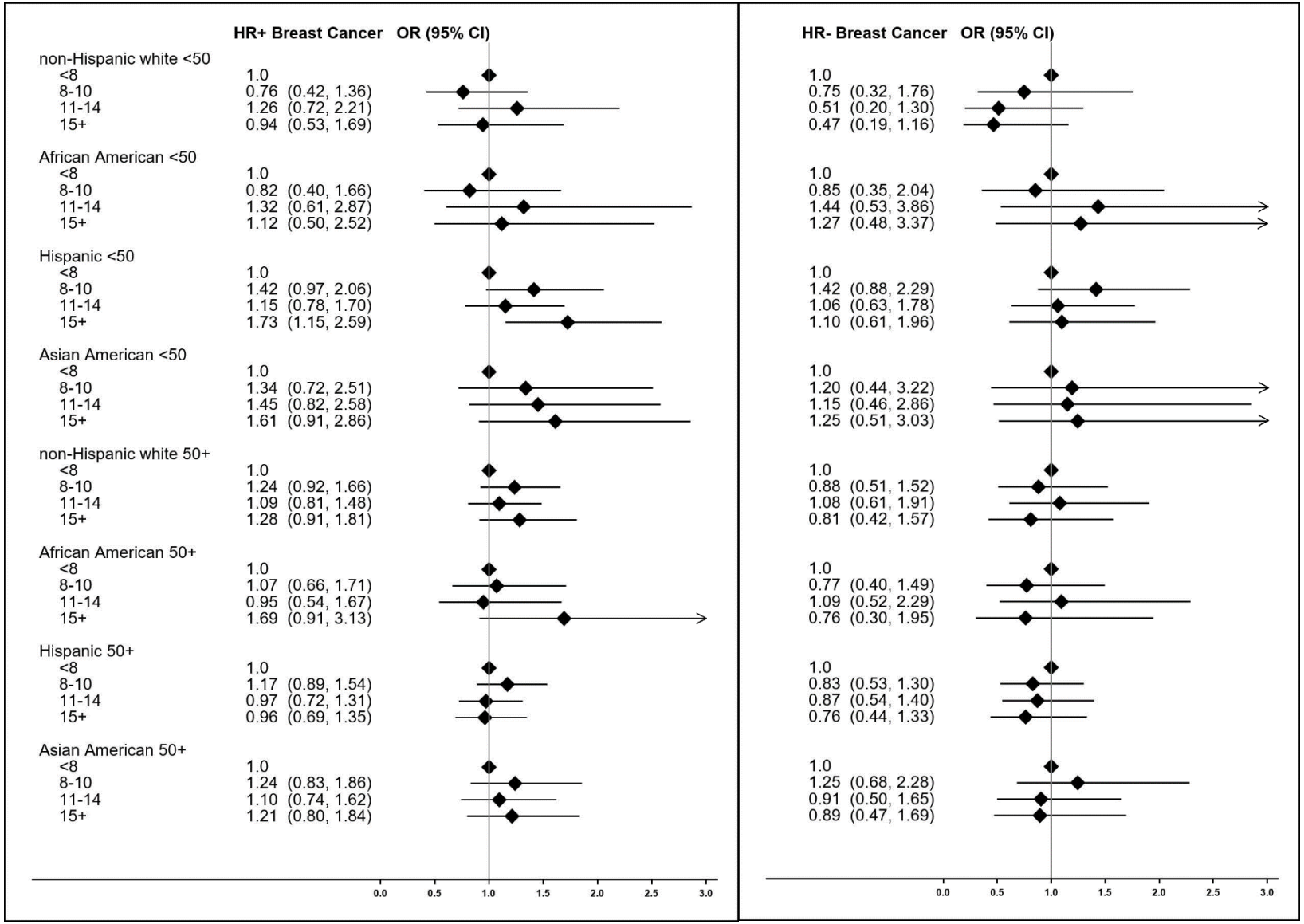
Supplemental Figure 2-D. Nulliparity and risk of breast cancer by hormone receptor status, race/ethnicity and age



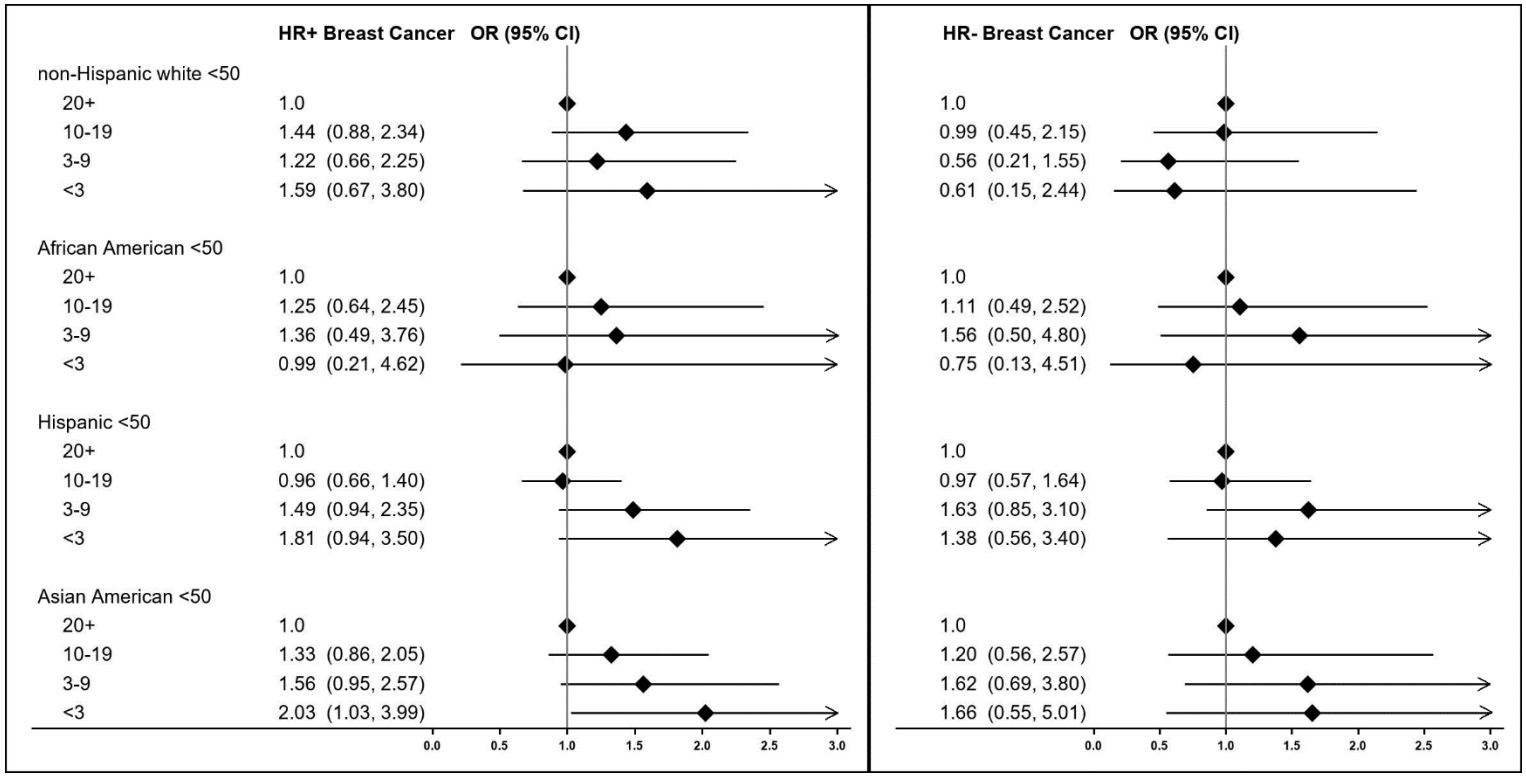
Supplemental Figure 2-E. Age at first full-term pregnancy and risk of breast cancer by hormone receptor status, race/ethnicity and age, parous women



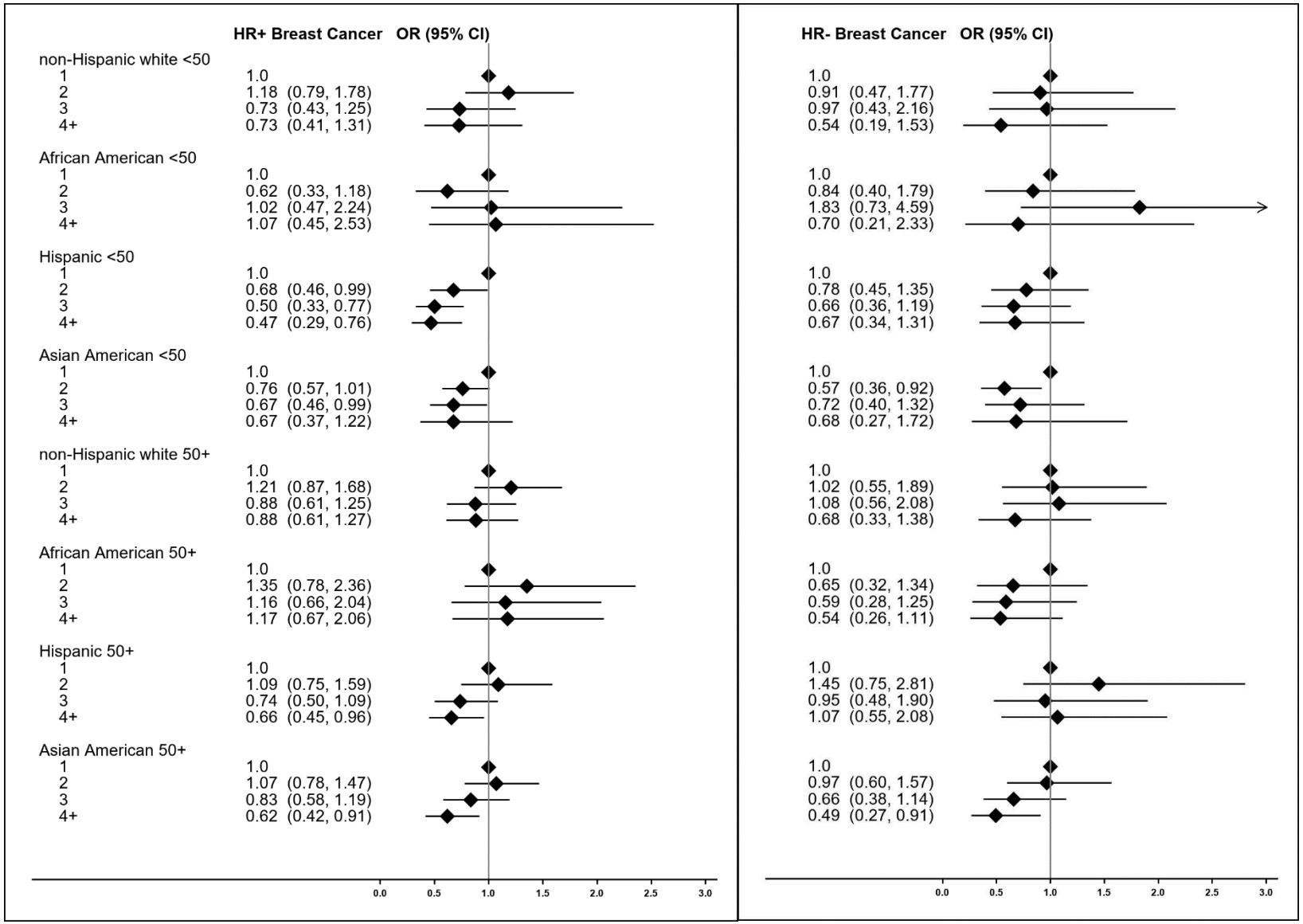
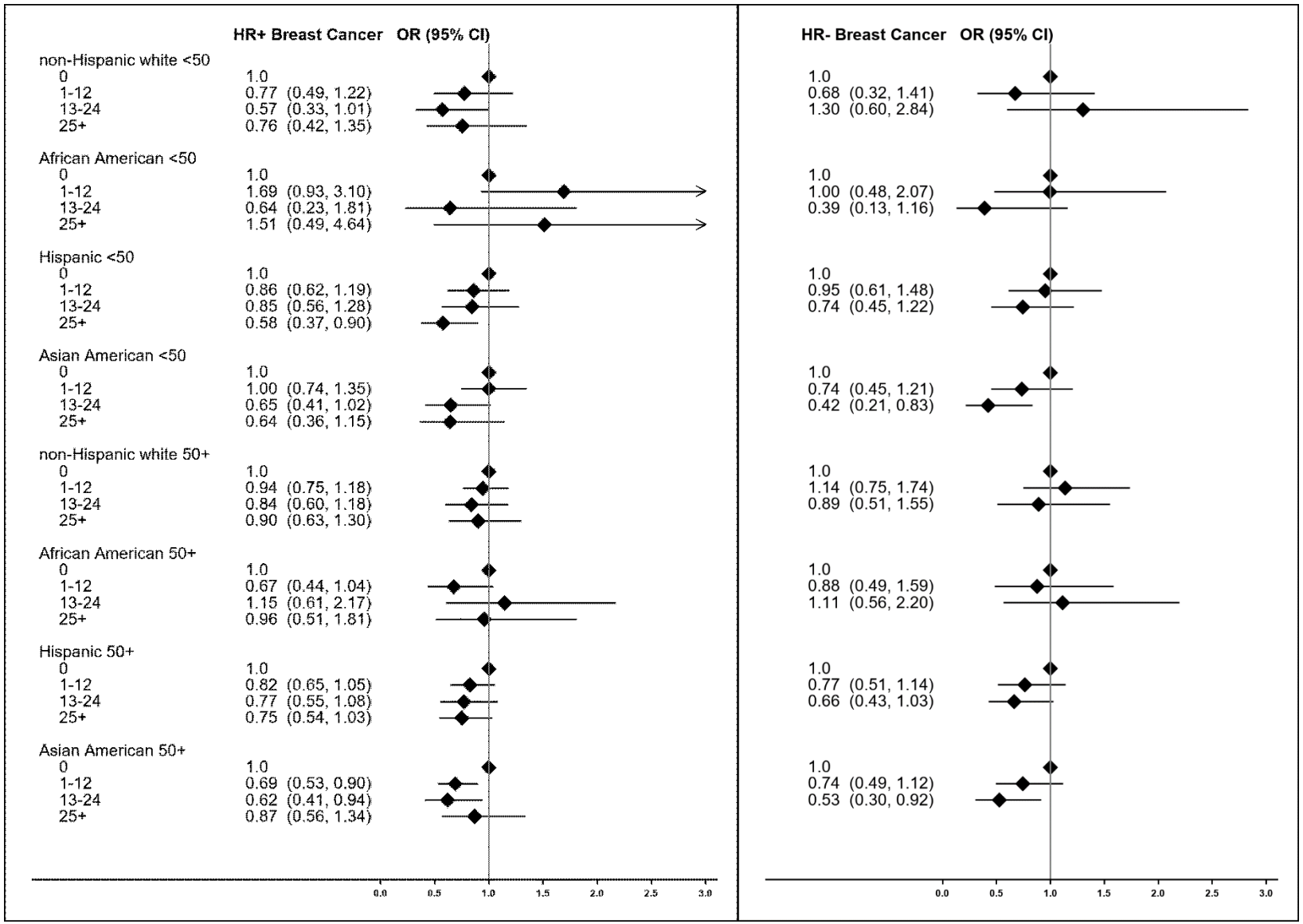
Supplemental Figure 2-F. Interval (years) between menarche and first full-term pregnancy and risk of breast cancer by hormone receptor status, race/ethnicity and age, parous women



Supplemental Figure 2-G. Time (years) since last full-term pregnancy and risk of breast cancer by hormone receptor status, race/ethnicity and age, parous women ages <50 years



Supplemental Figure 2-H. Parity (number of full-term pregnancies) and risk of breast cancer by hormone receptor status, race/ethnicity and age



Supplemental Figure 2-I. Lifetime breast-feeding (months) and risk of breast cancer by hormone receptor status, race/ethnicity and age, parous women. For HR- breast cancer, high category is ≥13 months.