Web Appendix

Example of Coding for Proportional Hazards Model in Equations 4 - 9.

```
*Let case = 1 if breast cancer, = 0 else.

    w1 = 1 if ER+, = 0 if ER-

    w2 = 1 if PR+, = 0 if PR-

    x1 = age

    x2 = parity

    yrs = follow-up time in years

*

If  w1 = 1 and w2 = 1 then type1=1; else type1 = 0;

If  w1 = 1 and w2 = 0 then type2=1; else type2 = 0;

If  w1 = 0 and w2 = 0 and case = 1 then type3=1; else type3 = 0;



array main age parity;

array er age_er parity_er;

array pr age_pr parity_pr;
```

```
status = type1;

type = 1;

do over main;

    er = main;

    pr = main;

end;

    output;

status = type2;

type = 2;

do over main;

    er = main;

    pr = 0;

end;

    output;

status = type3;
```

```
type = 3;

do over main;

    er = 0;

    pr = 0;

end;

    output;

* main effects model;

    proc phreg;

    model yrs*status(0) = age parity age_er parity_er age_pr
    parity_pr;

    strata type;



    test1: test age + age_er + age_pr = 0/print;

    test2: test age + age_er = 0/print;

    test3: test age = 0/print;
```

```
* test1, test2, test3, test the hypothesis that age has an effect on
ER+/PR+, ER+/PR-, and ER-/PR- breast cancer respectively;

test4: test age + age_er + 0.65 * age_pr = 0/print;

test5: test age + 0.65 * age_pr = 0/print;

test6: test age + age_pr + 0.81 * age_er = 0/print;

test7: test age + 0.81 * age_er = 0/print;

* test4, test5 estimate the effects of age for ER+ and ER- tumors,
respectively, adjusting for PR status, assuming that 65% of tumors
overall are PR+ (equation 7);

* test6, test7 estimate the effects of age for PR+ and PR- tumors,
respectively, adjusting for ER status, assuming that 81% of tumors
overall are ER+ (equation 7);

* heterogeneity of the effects estimated by test4 and test5 are
assessed by testing the hypothesis H0: β_age_er = 0 vs. H1: β_age_er ≠ 0;

* heterogeneity of the effects estimated by test6 and test7 are
assessed by testing the hypothesis H0: β_age_pr = 0 vs. H1: β_age_pr ≠ 0;
```

Web Table 1. Relationship Between Breast Cancer Risk Factor and Breast Cancer According to ER/PR Subtype, Nurses' Health Study 1980 – 2006, Boston, MA, USA.

	ER+/PR+ n = 2,125			ER+/PR- n = 540			ER-/PR- n = 627		
Variable	**β**	**SE**	***P* value**	**β**	**SE**	***P* value**	**β**	**SE**	***P* value**
Duration of Premenopause	0.091	0.007	< 0.001	0.097	0.015	< 0.001	0.043	0.013	< 0.001
Duration of Menopause									
Natural	0.036	0.004	< 0.001	0.042	0.008	< 0.001	0.022	0.008	0.005
Bilateral oophorectomy	0.030	0.006	< 0.001	0.034	0.011	0.003	0.027	0.010	0.007
Pregnancy History									
Gynecologic age at first birth (yrs)[a]	-0.003	0.004	0.48	0.021	0.009	0.020	0.018	0.009	0.051
Birth Index	-0.0036	0.0007	< 0.001	-0.0032	0.0014	0.017	0.0002	0.0013	0.88
Benign breast disease (BBD)									
BBD (yes vs. no)	0.663	0.499	0.18	0.753	0.999	0.45	0.178	0.873	0.84
BBD x age at menarche	0.042	0.023	0.068	0.048	0.045	0.28	0.020	0.043	0.65
BBD x duration premenopause	-0.015	0.009	0.11	-0.020	0.019	0.29	0.000	0.016	1.00

BBD x duration postmenopause	-0.023	0.005	< 0.001	-0.014	0.010	0.15	-0.002	0.009	0.79
Hormone Therapy use (HT)									
Duration, oral estrogen alone	0.023	0.007	0.002	0.014	0.014	0.31	0.004	0.014	0.76
Duration, oral estrogen plus progesterone	0.062	0.008	< 0.001	0.019	0.018	0.29	0.028	0.018	0.12
Duration, other types of hormones	0.025	0.009	0.003	-0.007	0.018	0.72	0.013	0.017	0.46
Current Use	0.294	0.066	< 0.001	0.319	0.132	0.016	0.114	0.125	0.36
Past Use	-0.183	0.067	0.007	0.026	0.127	0.84	-0.234	0.124	0.060
Body mass index (BMI), kg/m^2									
Estrogen Positive[b]	-0.0006	0.0002	0.006	-0.0017	0.0005	< 0.001	-0.0008	0.0004	0.042
Estrogen Negative[c]	0.0036	0.0005	< 0.001	0.0015	0.0010	0.16	0.0003	0.0010	0.79
Height (in)									
Estrogen Positive[b]	0.0011	0.0003	< 0.001	0.0001	0.0006	0.87	-0.0002	0.0005	0.70
Estrogen Negative[c]	-0.0001	0.0011	0.90	-0.0009	0.0021	0.66	0.0036	0.0020	0.072

Alcohol consumption (gm)[d]									
Premenopause	0.00047	0.00012	< 0.001	0.00056	0.00023	0.014	0.00044	0.00023	0.064
Postmenopause on pmh	-0.00011	0.00031	0.71	-0.00012	0.00063	0.85	-0.00171	0.00084	0.042
Postmenopause not on pmh	0.00037	0.00023	0.11	0.00015	0.00044	0.74	-0.00008	0.00047	0.86
Family history of breast cancer in a 1st degree relative	0.412	0.057	< 0.001	0.506	0.109	< 0.001	0.387	0.107	< 0.001

BBD, benign breast disease; BMI, body mass index; ER, estrogen receptor; HT, hormone therapy; PR, progesterone receptor.

[a] age at 1st birth – age at menarche
[b] BMI_estrogen positive = $BMI_1/100$; height_estrogen positive = $h_1/100$. Estrogen positive person time includes premenopausal person-time and postmenopausal person-time while on HT
[c] BMI_estrogen negative = $BMI_2/100$; height_estrogen negative = $h_2/100$. Estrogen negative person time includes postmenopausal person-time while not on HT.
[d] Alcohol_premenopause = $alc_1/100$; alcohol_postmenopause on pmh = $alc_2/100$; alcohol_postmenopause not on pmh = $alc_2/100$.

Web Table 2. Effects of Breast Cancer Risk Factors by ER, PR and HER2 Subtype, Adjusted for Other Tumor Markers, Cox Proportional Hazards Model, Nurses' Health Study 1980 – 2006, Case Subtypes Assessed by TMA, n = 1,331 Cases, Boston, MA, USA.

			ER			PR			HER2		
Variable	**Increment[a]**	**Subtype**	**HR**	**95% CI**	**P-value**	**HR**	**95% CI**	**P-value**	**HR**	**95% CI**	**P-value**
Duration of	1	+	1.09	1.07, 1.11	< 0.001	1.08	1.06, 1.11	< 0.001	1.06	1.01, 1.11	0.017
Premenopause		-	1.05	1.01, 1.10	0.028	1.07	1.04, 1.11	< 0.001	1.08	1.06, 1.10	<0.001
(yrs)					0.22[b]			0.76[b]			0.42[b]
Duration post											
Menopause (yrs)											
Natural	1	+	0.99	0.98, 1.01	0.23	0.98	0.96, 1.00	0.018	1.00	0.97, 1.03	0.88
		-	0.96	0.93, 0.99	0.008	0.99	0.97, 1.01	0.44	0.98	0.96, 0.99	<0.001
					0.065[b]			0.49[b]			0.11[b]
Bilateral	1	+	1.00	0.98, 1.02	0.98	0.96	0.94, 0.98	0.001	0.98	0.94, 1.03	0.47
oophorectomy		-	0.93	0.89, 0.97	<0.001	1.03	1.00, 1.06	0.031	0.98	0.96, 1.00	0.029
					0.87[b]			<0.001[b]			0.84[b]
Pregnancy History											
Gynecologic	22	+	1.57	1.14, 2.18	0.006	1.40	0.97, 2.01	0.073	0.93	0.46, 1.88	0.84
age at first birth		-	1.50	0.72, 3.18	0.28	1.42	1.09, 3.36	0.031	1.70	1.26, 2.29	0.029
(yrs)[c]					0.92[b]			0.41[b]			0.13[b]
Birth Index	102	+	0.70	0.56, 0.90	0.002	0.75	0.59, 0.97	0.026	0.86	0.55, 1.34	0.51
		-	0.94	0.57, 1.50	0.95	0.74	0.50, 1.10	0.13	0.72	0.59, 0.89	0.002
					0.35[b]			0.94[b]			0.50[b]
Benign breast											
disease (BBD)											
(present vs. absent)											

Age 50	1	+	1.57	1.29, 1.91	<0.001	1.61	1.30, 2.01	<0.001	2.27	1.50, 3.44	<0.001
		-	1.21	0.79, 1.86	0.38	1.26	0.90, 1.78	0.18	1.37	1.15, 1.63	<0.001
					0.32 [b]			0.30 [b]			0.028 [b]
Age 70	1	+	1.01	0.79, 1.28	0.95	1.00	0.75, 1.32	0.98	0.91	0.54, 1.56	0.74
		-	1.30	0.75, 2.25	0.5	1.21	0.82, 1.79	0.33	1.05	0.83, 1.34	0.66
					0.43 [b]			0.46 [b]			0.63 [b]
Hormone Therapy use (HT)											
oral estrogen (yrs)											
Current user	10	+	1.34	1.02, 1.76	0.035	2.29	1.68, 3.13	<0.001	1.13	0.60, 2.11	0.71
		-	2.80	1.55, 5.03	<0.001	0.76	0.48, 2.20	0.24	1.56	1.20, 2.01	<0.001
					0.038 [b]			<0.001 [b]			0.35 [b]
Past user	10	+	0.99	0.71, 1.37	0.95	1.40	0.95, 2.05	0.090	1.00	0.48, 2.10	0.49
		-	1.48	0.71, 3.10	0.30	0.66	0.38, 1.14	0.13	1.09	0.80, 1.50	0.58
					0.36 [b]			0.046 [b]			0.83 [b]
oral estrogen & progesterone (yrs)											
Current user	10	+	0.76	0.51, 1.15	0.20	1.13	0.75, 1.71	0.56	1.16	0.58, 2.34	0.67
		-	0.74	0.27, 2.01	0.56	0.35	0.16, 0.76	0.008	0.61	0.41, 0.91	0.016
					0.96 [b]			0.020 [b]			0.12 [b]
Past user	10	+	0.56	0.35, 0.90	0.016	0.69	0.43, 1.11	0.12	1.04	0.46, 2.33	0.93
		-	0.39	0.13, 1.21	0.10	0.30	0.13, 0.71	0.006	0.43	0.27, 0.68	<0.001
					0.59 [b]			0.14 [b]			0.064 [b]
Other types of hormones (yrs)											
Current user	10	+	0.90	0.64, 1.28	0.56	1.13	0.75, 1.71	0.56	0.68	0.30, 1.55	0.36

		-	1.24	0.57, 2.68	0.59	0.71	0.41, 1.25	0.24	0.99	0.71, 1.39	0.97
					0.49 [b]			0.24 [b]			0.40 [b]
Past user	10	+	0.67	0.45, 0.99	0.043	0.69	0.43, 1.11	0.12	0.60	0.24, 1.51	0.28
		-	0.66	0.27, 1.60	0.36	0.62	0.33, 1.17	0.14	0.70	0.48, 1.02	0.066
					0.97 [b]			0.81 [b]			0.77 [b]
Body mass index (BMI) (kg/m^2)											
Age 50	8	+	0.64	0.52, 0.79	<0.001	0.71	0.56, 0.89	0.004	0.71	0.45, 1.11	0.13
		-	0.74	0.46, 1.19	0.22	0.58	0.39, 0.86	0.006	0.67	0.55, 0.81	<0.001
					0.63 [b]			0.45 [b]			0.84 [b]
Age 70	8	+	0.86	0.66, 1.13	0.29	1.16	0.84, 1.59	0.37	1.22	0.71, 2.09	0.46
		-	0.80	0.39, 1.63	0.54	0.46	0.28, 0.76	0.002	0.84	0.64, 1.10	0.19
					0.86 [b]			0.006 [b]			0.22 [b]
Height (in.)											
Age 50	6	+	1.19	0.97, 1.44	0.090	1.24	1.00, 1.54	0.052	0.80	0.52, 1.22	0.31
		-	1.13	0.74, 1.75	0.57	1.05	0.74, 1.49	0.76	1.19	0.97, 1.44	0.090
					0.87 [b]			0.50 [b]			0.055 [b]
Age 70	6	+	1.10	0.76, 1.60	0.60	1.68	1.07, 2.64	0.024	1.30	0.58, 2.89	0.52
		-	2.58	1.10, 6.08	0.030	0.85	0.47, 1.55	0.59	1.10	0.76, 1.60	0.60
					0.089 [b]			0.10 [b]			0.97 [b]
Alcohol (gm)											
Age 50	11	+	1.09	0.97, 1.23	0.16	0.97	0.84, 1.14	0.74	1.21	0.97, 1.51	0.088
		-	0.82	0.60, 1.10	0.19	1.12	0.92, 1.36	0.25	0.97	0.85, 1.11	0.68
					0.088 [b]			0.30 [b]			0.094 [b]
Age 70	11	+	1.20	1.02, 1.41	0.031	1.10	0.90, 1.35	0.36	1.34	0.97, 1.84	0.078
		-	0.88	0.58, 1.34	0.54	1.15	0.88, 1.49	0.30	1.05	0.88, 1.26	0.56

					0.19 [b]			0.81 [b]			0.21 [b]
Family history of	1	+	1.43	1.19, 1.72	<0.001	1.35	1.09, 1.68	0.005	1.20	0.78, 1.83	0.41
breast cancer		-	1.36	0.90, 2.07	0.15	1.55	1.13, 2.12	0.007	1.49	1.26, 1.77	<0.001
					0.84 [b]			0.54 [b]			0.35 [b]

BBD, benign breast disease; BMI, body mass index; CI, confidence interval; ER, estrogen receptor; HER2, Human Epidermal growth factor Receptor 2; HR, hazard ratio; HT, hormone therapy; PR, progesterone receptor; TMA, tumor tissue microarray.

[a] Increment: duration of premenopause, duration of menopause, 1 yr; gynecologic age at 1st birth, 22 (35-13) yrs vs. nulliparous; birth index, 102 (4 births at ages 20, 23, 26, 29) vs. nulliparous; benign breast disease, family history, present vs. absent; hormone therapy, 10 yrs of use vs. 0 yrs of use; body mass index, 8 kg/m^2 (30 kg/m^2 vs. 22 kg/m^2); height 6 in. (5'10" vs. 5'4"); alcohol (11 gm, 1 drink per day vs. 0 drinks per day starting at age 18). All comparisons assume age at menarche = 13 and age at natural menopause = 50; HR for Body mass index, height and alcohol assume no HT use

[b] P value for heterogeneity comparing subtype + vs. subtype -

[c] age at 1st birth – age at menarche

Web Table 3. Effects of Breast Cancer Risk Factors by ER, PR and HER2 Subtype, Adjusted for Other Tumor Markers and Tumor Size[a], Cox Proportional Hazards' Model, Nurses' Health Study, 1980-2006, Boston, MA, USA.

			ER			PR			HER2			Tumor size		
Variable	**Increment[b]**	**subtype**	**HR**	**95% CI**	**P-value**	**HR**	**95% CI**	**P-value**	**HR**	**95% CI**	**P-value**	**HR**	**95% CI**	**P-value**
Duration of	1	+	1.10	1.08, 1.11	<0.001	1.08	1.07, 1.10	<0.001	1.08	1.03, 1.14	<0.001	1.09	1.07, 1.11	<0.001
Premenopause		-	1.04	1.01, 1.08	0.019	1.09	1.07, 1.12	<0.001	1.09	1.07, 1.11	<0.001	1.09	1.07, 1.10	<0.001
(yrs)					<0.008[c]			0.56[c]			0.86[c]			0.95[c]
Duration of Menopause (yrs)														
Natural	1	+	1.04	1.03, 1.05	<0.001	1.03	1.02, 1.04	<0.001	1.05	1.03, 1.08	<0.001	1.02	1.00, 1.03	0.014
		-	1.02	1.01, 1.08	0.019	1.04	1.03, 1.05	<0.001	1.02	1.01, 1.03	0.002	1.04	1.04, 1.05	<0.001
					0.12[c]			0.50[c]			0.020[c]			<0.001[c]
Bilateral	1	+	1.03	1.02, 1.04	<0.001	1.03	1.02, 1.04	<0.001	1.04	1.01, 1.08	0.014	1.02	1.00, 1.04	0.047
oophorectomy		-	1.03	1.00, 1.05	0.045	1.04	1.02, 1.05	<0.001	1.02	1.01, 1.04	0.003	1.05	1.02, 1.08	0.001
					0.72[c]			0.67[c]			0.21[c]			0.067[c]
Pregnancy History														
Gynecologic	22	+	1.14	0.94, 1.38	0.17	0.94	0.91, 1.18	0.58	1.22	0.64, 2.34	0.55	1.26	0.93, 1.69	0.13
age at first		-	1.03	0.63, 1.69	0.91	1.54	1.11, 2.15	0.010	1.39	1.05, 1.84	0.020	1.07	0.88, 1.30	0.52
birth (yrs)[d]					0.72[c]			0.028[c]			0.71[c]			0.37[c]
Birth Index	102	+	0.71	0.62, 0.81	<0.001	0.76	0.65, 0.88	<0.001	0.89	0.59, 1.34	0.58	0.67	0.54, 0.82	<0.001
		-	1.02	0.74, 1.41	0.88	0.77	0.61, 0.96	0.023	0.83	0.69, 1.00	0.051	0.80	0.71, 0.91	<0.001
					0.055[c]			0.92[c]			0.78[c]			0.14[c]
Benign breast disease (BBD) (present vs. absent)														
Age 50	1	+	1.89	1.63, 2.17	<0.001	1.84	1.56, 2.17	<0.001	2.14	1.32, 3.48	0.002	1.62	1.32, 1.98	<0.001
		-	1.54	1.10, 2.16	0.011	1.77	1.39, 2.27	<0.001	1.73	1.43, 2.09	<0.001	1.91	1.65, 2.20	<0.001
					0.32[c]			0.83[c]			0.42[c]			0.19[c]

Age 70	1	+	1.32	1.17, 1.48	<0.001	1.25	1.09, 1.43	0.002	1.61	1.13, 2.29	0.009	1.48	1.22,1.80	<0.001
		-	1.30	0.97, 1.75	0.078	1.44	1.18, 1.75	<0.001	1.22	1.03, 1.44	0.021	1.25	1.11, 1.40	<0.001
					0.96[c]			0.29[c]			0.17[c]			0.15[c]
Hormone Therapy use (HT)														
oral estrogen (yrs)														
Current	10	+	1.64	1.41, 1.91	<0.001	1.59	1.33, 1.89	<0.001	1.06	0.64, 1.76	0.81	1.17	0.92, 1.50	0.20
user		-	1.28	0.89, 1.86	0.19	1.53	1.19, 1.98	<0.001	1.21	0.97, 1.50	0.092	1.77	1.53, 2.05	<0.001
					0.26[c]			0.85[c]			0.66[c]			0.005[c]
Past user	10	+	1.06	0.89, 1.27	0.51	0.95	0.77, 1.18	0.66	0.94	0.53, 1.65	0.82	0.80	0.60, 1.08	0.14
		-	0.78	0.50, 1.22	0.27	1.09	0.81, 1.48	0.55	1.39	1.08, 1.78	0.009	1.10	0.92, 1.31	0.30
					0.24[c]			0.50[c]			0.21[c]			0.073[c]
oral estrogen & progesterone (yrs)														
Current	10	+	2.09	1.78, 2.46	<0.001	2.46	2.04, 2.97	<0.001	2.05	1.26, 3.34	0.004	1.41	1.07, 1.86	0.015
user		-	2.18	1.43, 3.31	<0.001	1.59	1.19, 2.12	0.002	1.73	1.37, 2.18	<0.001	2.50	2.14, 2.92	<0.001
					0.88[c]			0.023[c]			0.54[c]			<0.001[c]
Past user	10	+	1.35	1.12, 1.64	0.002	1.48	1.19, 1.85	<0.001	1.80	1.04, 3.12	0.036	0.96	0.70, 1.33	0.83
		-	1.32	0.81, 2.16	0.26	1.14	0.82, 1.58	0.45	1.99	1.53, 2.58	<0.001	1.55	1.29, 1.87	<0.001
					0.93[c]			0.24[c]			0.75[c]			0.012[c]
other types of hormones (yrs)														
Current	10	+	1.56	1.32, 1.85	<0.001	1.76	1.45, 2.14	<0.001	1.45	0.87, 2.43	0.15	1.29	0.99, 1.69	0.062
user		-	1.65	1.09, 2.52	0.019	1.30	0.96, 1.75	0.087	1.26	0.99, 1.60	0.066	1.72	1.45, 2.03	<0.001
					0.82[c]			0.13[c]			0.61[c]			0.079[c]
Past user	10	+	1.01	0.83, 1.23	0.92	1.06	0.84, 1.33	0.64	1.28	0.72, 2.27	0.40	0.88	0.65, 1.21	0.44
		-	1.00	0.62, 1.63	0.98	0.93	0.66, 1.30	0.66	1.45	1.11, 1.89	0.007	1.07	0.88, 1.29	0.52
					0.99[c]			0.57[c]			0.70[c]			0.32[c]

Body mass index (BMI) (kg/m^2)														
Age 50	8	+	0.75	0.66, 0.85	<0.001	0.90	0.78, 1.04	0.15	0.92	0.62, 1.36	0.67	0.82	0.68, 0.99	0.039
		-	0.98	0.72, 1.35	0.91	0.63	0.50, 0.79	<0.001	0.78	0.66, 0.93	0.005	0.78	0.69, 0.88	<0.001
					0.16[c]			0.019[c]			0.47[c]			0.65[c]
Age 70	8	+	1.20	1.04, 1.37	0.010	1.52	1.30, 1.78	<0.001	1.38	0.92, 2.09	0.12	1.33	0.98, 1.82	0.069
		-	1.20	0.83, 1.73	0.33	0.77	0.60, 0.99	0.043	1.14	0.94, 1.38	0.19	0.94	0.71, 1.26	0.69
					0.99[c]			<0.001[c]			0.40[c]			0.005[c]
Height (in.)														
Age 50	6	+	1.17	1.04, 1.32	0.010	1.29	1.12, 1.48	<0.001	0.89	0.60, 1.32	0.57	1.13	0.94, 1.36	0.20
		-	1.20	0.89, 1.62	0.22	1.00	0.81, 1.23	0.99	1.19	1.01, 1.41	0.038	1.20	1.06, 1.35	0.003
					0.87[c]			0.076[c]			0.18[c]			0.60[c]
Age 70	6	+	1.09	0.90, 1.31	0.40	1.33	1.06, 1.67	0.015	1.65	0.92, 2.94	0.092	1.09	0.80, 1.48	0.58
		-	1.70	1.05, 2.75	0.030	0.96	0.69, 1.32	0.78	1.12	0.85, 1.49	0.42	1.22	1.01, 1.49	0.041
					0.11[c]			0.14[c]			0.24[c]			0.53[c]
Alcohol (gm)														
Age 50	11	+	1.20	1.11, 1.30	<0.001	1.18	1.07, 1.29	<0.001	1.30	1.03, 1.64	0.027	1.18	1.04, 1.34	0.009
		-	1.15	0.94, 1.41	0.16	1.22	1.07, 1.39	0.003	1.09	0.97, 1.23	0.15	1.20	1.11, 1.30	<0.001
					0.72[c]			0.71[c]			0.19[c]			0.84[c]
Age 70	11	+	1.26	1.15, 1.39	<0.001	1.23	1.05, 1.44	0.012	1.24	0.92, 1.66	0.16	1.19	1.00, 1.43	0.055
		-	1.14	0.89, 1.46	0.31	1.21	1.04, 1.42	0.016	1.19	1.04, 1.37	0.15	1.26	1.09, 1.46	0.002
					0.46[c]			0.74[c]			0.84[c]			0.56[c]
Family history of breast cancer		+	1.56	1.40, 1.73	<0.001	1.48	1.30, 1.68	<0.001	1.76	1.25, 2.47	0.001	1.22	1.02, 1.47	0.031
		-	1.40	1.07, 1.83	0.015	1.61	1.34, 1.93	<0.001	1.51	1.30, 1.76	<0.001	1.67	1.50, 1.86	<0.001
					0.50[c]			0.52[c]			0.43[c]			0.004[c]

BBD, benign breast disease; BMI, body mass index; ER, estrogen receptor; HER2, Human Epidermal growth factor Receptor 2; HT, hormone therapy; PR, progesterone receptor.
[a] Tumor size: small if ≤2cm; large if >2cm.
[b] Increment: duration of premenopause, duration of menopause, 1 yr; gynecologic age at 1st birth, 22 (35-13) yrs vs. nulliparous; birth index, 102 (4 births at ages 20, 23, 26, 29) vs. nulliparous; benign breast disease, family history, present vs. absent; hormone therapy, 10 yrs of use vs. 0 yrs of use; body mass index, 8 kg/m^2 (30 kg/m^2 vs. 22 kg/m^2); height 6 in. (5'10" vs. 5'4"); alcohol (11 gm, 1 drink per day vs. 0 drinks per day starting at age 18). All comparisons assume age at menarche = 13 and age at natural menopause = 50; HR for Body mass index, height and alcohol assume no HT use
[c] P-value for heterogeneity comparing subtype + vs. subtype -
[d] age at 1st birth – age at menarche