Table S1: Breast cancer hazard ratios by serum iron covariate (restricted to first four years of follow-up)

Biomarkers	Quartile of iron-related biomarker				Linear trend over quartiles[c]
	Quartile 1	Quartile 2	Quartile 3	Quartile 4	
Iron (μg/dL)					
Median	63	85	103	133	
Ranges	[5,74]	(74,93]	(93,115]	(115,340]	
Unadjusted	ref	1.00 (0.83, 1.21)	1.02 (0.85, 1.24)	1.08 (0.90, 1.31)	1.03 (0.97, 1.09)
Adjusted[a]	ref	0.98 (0.80, 1.21)	1.04 (0.84, 1.28)	1.03 (0.84, 1.27)	1.01 (0.95, 1.08)
Ferritin[b] (μg/dL)					
Median	21	50	87	157	
Ranges	[5,36]	(36,67]	(67,113]	(113,1625]	
Unadjusted	ref	0.93 (0.77, 1.13)	0.95 (0.78, 1.15)	1.02 (0.84, 1.24)	1.01 (0.95, 1.08)
Adjusted[a]	ref	0.94 (0.76, 1.16)	0.99 (0.80, 1.22)	1.01 (0.81, 1.25)	1.01 (0.94, 1.08)
Transferrin saturation (%)					
Median	19	27	33	42	
Ranges	[2,23]	(23,29]	(29,36]	(36,90]	
Unadjusted	ref	1.01 (0.84, 1.22)	1.07 (0.88, 1.28)	1.03 (0.86, 1.24)	1.02 (0.96, 1.08)
Adjusted[a]	ref	0.96 (0.78, 1.17)	1.08 (0.88, 1.33)	0.94 (0.77, 1.16)	1.00 (0.93, 1.06)
First principal component[d]					
Median	-1.5	-0.3	0.6	1.5	
Ranges	[-9.82,-0.786]	(-0.786,0.156]	(0.156,0.977]	(0.977,5.11]	
Unadjusted	ref	1.06 (0.87, 1.28)	1.08 (0.89, 1.31)	1.08 (0.89, 1.31)	1.03 (0.97, 1.09)
Adjusted[a]	ref	1.02 (0.83, 1.26)	1.04 (0.85, 1.29)	1.00 (0.81, 1.24)	1.00 (0.94, 1.07)

[a] Adjusted for baseline smoking, alcohol, education, HRT, age at menarche, age at first birth, oral contraceptive use, menopause status, BMI, and a product term between the last two variables.

[b] log transformed

[c] Iron covariate in quartile units

[d] The first principal component explains 72% of the variance and represents loadings of 0.63, 0.40, and 0.66 for the iron, ferritin and transferrin saturation measures, respectively.

Table S2: Breast cancer hazard ratios by serum iron covariate (omitting first two years of follow-up)

	Quartile of iron-related biomarker				Linear trend over quartiles[c]
Biomarkers	Quartile 1	Quartile 2	Quartile 3	Quartile 4	
Iron (μg/dL)					
Median	63	84	103	133	
Ranges	[5,74]	(74,93]	(93,115]	(115,340]	
Unadjusted	ref	1.12 (0.96, 1.31)	1.11 (0.95, 1.31)	1.09 (0.93, 1.28)	1.02 (0.97, 1.08)
Adjusted[a]	ref	1.14 (0.95, 1.35)	1.16 (0.97, 1.38)	1.10 (0.92, 1.32)	1.03 (0.97, 1.09)
Ferritin[b] (μg/dL)					
Median	22	51	88	156	
Ranges	[5,36]	(36,67]	(67,113]	(113,1404]	
Unadjusted	ref	1.00 (0.85, 1.17)	1.06 (0.90, 1.25)	1.11 (0.94, 1.31)	1.04 (0.99, 1.09)
Adjusted[a]	ref	1.00 (0.83, 1.19)	1.07 (0.89, 1.28)	1.07 (0.89, 1.29)	1.03 (0.97, 1.09)
Transferrin saturation (%)					
Median	19	26	33	42	
Ranges	[2,22]	(22,29]	(29,36]	(36,87]	
Unadjusted	ref	0.97 (0.83, 1.13)	1.05 (0.90, 1.24)	0.99 (0.84, 1.17)	1.01 (0.96, 1.06)
Adjusted[a]	ref	0.94 (0.79, 1.11)	1.10 (0.92, 1.31)	0.98 (0.82, 1.17)	1.01 (0.95, 1.07)
First principal component[d]					
Median	-1.5	-0.3	0.6	1.5	
Ranges	[-9.93,-0.799]	(-0.799,0.146]	(0.146,0.979]	(0.979,5.13]	
Unadjusted	ref	1.14 (0.97, 1.33)	1.06 (0.90, 1.24)	1.10 (0.93, 1.29)	1.02 (0.97, 1.07)
Adjusted[a]	ref	1.18 (0.99, 1.40)	1.04 (0.88, 1.25)	1.11 (0.93, 1.33)	1.02 (0.96, 1.08)

[a] Adjusted for baseline smoking, alcohol, education, HRT, age at menarche, age at first birth, oral contraceptive use, menopause status, BMI, and a product term between the last two variables.

[b] log transformed

[c] Iron covariate in quartile units

[d] The first principal component explains 72% of the variance and represents loadings of 0.63, 0.40, and 0.66 for the iron, ferritin and transferrin saturation measures, respectively.

Table S3: Breast cancer hazard ratios by serum iron covariate and race/ethnic subgroups.

			Quartile of iron-related biomarker				Linear trend over quartiles[c]
Iron	Race/ethnicity	Values	ref	Q2	Q3	Q4	
Iron (μg/dL)	Black, non-Hispanic (n=470, subcohort n=262)	Median	55	72	87	108	
		Ranges	[20,66]	(66,79]	(79,96.2]	(96.2,236]	
		Unadjusted HR (95% CI)	ref	1.00 (0.58, 1.73)	0.90 (0.53, 1.56)	1.08 (0.63, 1.86)	1.02 (0.86, 1.21)
		Adjusted[a] HR (95% CI)	ref	1.01 (0.58, 1.76)	0.92 (0.53, 1.59)	1.09 (0.63, 1.91)	1.02 (0.85, 1.21)
	Hispanic (n=236, subcohort n=135)	Median	66	85	102	136	
		Ranges	[21,74]	(74,92]	(92,114]	(114,223]	
		Unadjusted HR (95% CI)	ref	1.03 (0.48, 2.22)	0.58 (0.26, 1.27)	0.80 (0.38, 1.68)	0.88 (0.70, 1.12)
		Adjusted[a] HR (95% CI)	ref	1.01 (0.46, 2.20)	0.58 (0.26, 1.30)	0.79 (0.37, 1.69)	0.89 (0.69, 1.14)
	White, non-Hispanic (n=4881, subcohort n=2487)	Median	64	86	105	134	
		Ranges	[5,76]	(76,94]	(94,117]	(117,340]	
		Unadjusted HR (95% CI)	ref	1.13 (0.96, 1.33)	1.09 (0.93, 1.28)	1.13 (0.96, 1.32)	1.03 (0.98, 1.09)
		Adjusted[a] HR (95% CI)	ref	1.13 (0.96, 1.33)	1.11 (0.94, 1.30)	1.16 (0.98, 1.36)	1.04 (0.99, 1.10)
Ferritin[b] (μg/dL)	Black, non-Hispanic (n=470, subcohort n=262)	Median	19	56	102	189	
		Ranges	[5,38]	(38,82]	(82,134.2]	(134.2,832]	
		Unadjusted HR (95% CI)	ref	1.03 (0.60, 1.80)	1.17 (0.67, 2.02)	1.16 (0.66, 2.02)	1.06 (0.88, 1.26)
		Adjusted[a] HR (95% CI)	ref	1.06 (0.60, 1.87)	1.16 (0.65, 2.06)	1.17 (0.66, 2.06)	1.06 (0.88, 1.26)
	Hispanic (n=236, subcohort n=135)	Median	22	55	88	170	
		Ranges	[5,39]	(39,75]	(75,119.8]	(119.8,573]	
		Unadjusted HR (95% CI)	ref	0.51 (0.23, 1.12)	0.41 (0.18, 0.95)	0.90 (0.40, 2.05)	0.98 (0.75, 1.29)
		Adjusted[a] HR (95% CI)	ref	0.52 (0.22, 1.21)	0.38 (0.16, 0.92)	0.85 (0.36, 1.99)	0.96 (0.73, 1.27)
	White, non-Hispanic (n=4881, subcohort n=2487)	Median	22	50	86	152	
		Ranges	[5,36]	(36,66]	(66,111]	(111,1625]	
		Unadjusted HR (95% CI)	ref	1.08 (0.92, 1.27)	1.11 (0.94, 1.30)	1.07 (0.91, 1.27)	1.02 (0.97, 1.08)
		Adjusted[a] HR (95% CI)	ref	1.09 (0.92, 1.28)	1.11 (0.94, 1.31)	1.05 (0.89, 1.24)	1.02 (0.96, 1.07)
Transferrin Saturation (%)	Black, non-Hispanic (n=470, subcohort n=262)	Median	17	23	28	36	
		Ranges	[5,21]	(21,25]	(25,31]	(31,64]	
		Unadjusted HR (95% CI)	ref	1.04 (0.60, 1.81)	1.04 (0.62, 1.75)	0.94 (0.55, 1.59)	0.98 (0.83, 1.16)
		Adjusted[a] HR (95% CI)	ref	1.05 (0.60, 1.84)	1.04 (0.62, 1.75)	0.93 (0.54, 1.60)	0.98 (0.83, 1.16)
	Hispanic (n=236, subcohort n=135)	Median	20	26	32	42	
		Ranges	[5,23.2]	(23.2,29]	(29,35]	(35,66]	
		Unadjusted HR (95% CI)	ref	0.84 (0.39, 1.80)	0.87 (0.40, 1.87)	0.62 (0.29, 1.33)	0.87 (0.68, 1.11)
		Adjusted[a] HR (95% CI)	ref	0.81 (0.37, 1.77)	0.83 (0.37, 1.84)	0.61 (0.28, 1.36)	0.87 (0.68, 1.11)
	White, non-Hispanic (n=4881, subcohort n=2487)	Median	19	27	33	42	
		Ranges	[2,23]	(23,29]	(29,36]	(36,90]	
		Unadjusted HR (95% CI)	ref	1.07 (0.91, 1.25)	1.15 (0.98, 1.35)	1.05 (0.90, 1.22)	1.02 (0.97, 1.07)
		Adjusted[a] HR (95% CI)	ref	1.07 (0.91, 1.26)	1.17 (1.00, 1.38)	1.08 (0.92, 1.27)	1.03 (0.98, 1.09)
First principal component	Black, non-Hispanic (n=470, subcohort n=262)	Median	-2	-1	0	1	
		Ranges	[-6.89,-1.08]	(-1.08,-0.243]	(-0.243,0.467]	(0.467,3.39]	
		Unadjusted HR (95% CI)	ref	1.04 (0.60, 1.81)	1.23 (0.71, 2.11)	0.92 (0.53, 1.60)	0.99 (0.83, 1.18)
		Adjusted[a] HR (95% CI)	ref	1.04 (0.60, 1.82)	1.24 (0.71, 2.14)	0.91 (0.52, 1.60)	0.99 (0.83, 1.18)
	Hispanic (n=236, subcohort n=135)	Median	-1	-0	1	2	
		Ranges	[-6.64,-0.727]	(-0.727,0.204]	(0.204,1.04]	(1.04,2.99]	
		Unadjusted HR (95% CI)	ref	1.10 (0.51, 2.38)	0.71 (0.33, 1.55)	0.69 (0.32, 1.48)	0.86 (0.67, 1.09)
		Adjusted[a] HR (95% CI)	ref	1.05 (0.48, 2.32)	0.72 (0.33, 1.58)	0.69 (0.32, 1.50)	0.86 (0.67, 1.10)
	White, non-Hispanic (n=4881, subcohort n=2487)	Median	-2	-0	1	2	
		Ranges	[-9.9,-0.765]	(-0.765,0.192]	(0.192,1.02]	(1.02,5.12]	
		Unadjusted HR (95% CI)	ref	1.17 (1.00, 1.38)	1.14 (0.97, 1.34)	1.13 (0.97, 1.33)	1.04 (0.98, 1.09)
		Adjusted[a] HR (95% CI)	ref	1.17 (0.99, 1.37)	1.15 (0.97, 1.35)	1.16 (0.98, 1.36)	1.04 (0.99, 1.10)

[a] Adjusted for BMI, baseline menopause status, and a product term of these two variables. Number of adjusted factors is small due to small sample size for some groups.
[b] log transformed
[c] Iron covariate in quartile units

Table S4: Breast cancer hazard ratios by serum iron covariate and BMI subgroups

Iron	BMI groups	Values	Quartile of iron-related biomarker				Linear trend over quartiles[d]
			ref[c]	Q2	Q3	Q4	
Iron (μg/dL)	Normal: 18.5-24.9 (n=2094, subcohort n=1105)	Median	66	90	111	142	
		Ranges	[5,79]	(79,100]	(100,125]	(125,340]	
		Unadjusted HR (95% CI)	ref	1.02 (0.80, 1.30)	0.94 (0.73, 1.20)	1.07 (0.83, 1.36)	1.01 (0.94, 1.09)
		Adjusted[a] HR (95% CI)	ref	0.94 (0.72, 1.23)	0.90 (0.69, 1.17)	1.02 (0.78, 1.33)	1.00 (0.92, 1.09)
	Overweight: 25.0-29.9 (n=1839, subcohort n=942)	Median	64	86	104	133	
		Ranges	[21,76]	(76,94]	(94,114]	(114,332]	
		Unadjusted HR (95% CI)	ref	0.84 (0.65, 1.10)	1.02 (0.78, 1.33)	0.92 (0.70, 1.20)	0.99 (0.91, 1.08)
		Adjusted[a] HR (95% CI)	ref	0.82 (0.61, 1.10)	0.99 (0.74, 1.32)	0.81 (0.60, 1.09)	0.96 (0.87, 1.05)
	Obese: 30+ (n=1760, subcohort n=889)	Median	60	78	94	121	
		Ranges	[14,69]	(69,85]	(85,103]	(103,276]	
		Unadjusted HR (95% CI)	ref	1.47 (1.11, 1.93)	1.27 (0.97, 1.68)	1.27 (0.96, 1.67)	1.06 (0.97, 1.15)
		Adjusted[a] HR (95% CI)	ref	1.47 (1.08, 1.99)	1.34 (0.98, 1.82)	1.37 (1.01, 1.86)	1.08 (0.98, 1.19)
Ferritin[b] (μg/dL)	Normal: 18.5-24.9 (n=2094, subcohort n=1105)	Median	22	47	77	135	
		Ranges	[5,34]	(34,61]	(61,97]	(97,1625]	
		Unadjusted HR (95% CI)	ref	0.96 (0.75, 1.24)	1.02 (0.79, 1.32)	1.06 (0.82, 1.37)	1.02 (0.94, 1.11)
		Adjusted[a] HR (95% CI)	ref	0.86 (0.65, 1.12)	0.93 (0.70, 1.23)	0.99 (0.75, 1.32)	1.01 (0.92, 1.11)
	Overweight: 25.0-29.9 (n=1839, subcohort n=942)	Median	22	53	90	152	
		Ranges	[5,37]	(37,70]	(70,114]	(114,1160]	
		Unadjusted HR (95% CI)	ref	0.93 (0.71, 1.21)	1.03 (0.79, 1.35)	1.00 (0.76, 1.32)	1.01 (0.93, 1.10)
		Adjusted[a] HR (95% CI)	ref	0.96 (0.71, 1.29)	1.18 (0.87, 1.60)	1.06 (0.78, 1.44)	1.04 (0.94, 1.14)
	Obese: 30+ (n=1760, subcohort n=889)	Median	22	59	102	185	
		Ranges	[5,40]	(40,78.5]	(78.5,133]	(133,1404]	
		Unadjusted HR (95% CI)	ref	1.27 (0.97, 1.67)	1.15 (0.88, 1.52)	1.30 (0.98, 1.72)	1.07 (0.98, 1.17)
		Adjusted[a] HR (95% CI)	ref	1.22 (0.90, 1.65)	1.13 (0.83, 1.54)	1.20 (0.88, 1.65)	1.05 (0.95, 1.16)
Transferrin Saturation (%)	Normal: 18.5-24.9 (n=2094, subcohort n=1105)	Median	20	28	35	45	
		Ranges	[2,24]	(24,31]	(31,39]	(39,90]	
		Unadjusted HR (95% CI)	ref	1.20 (0.94, 1.54)	1.03 (0.81, 1.31)	1.17 (0.92, 1.50)	1.03 (0.96, 1.12)
		Adjusted[a] HR (95% CI)	ref	1.07 (0.82, 1.39)	0.93 (0.72, 1.21)	1.07 (0.82, 1.40)	1.01 (0.93, 1.10)
	Overweight: 25.0-29.9 (n=1839, subcohort n=942)	Median	20	26	33	42	
		Ranges	[5,23]	(23,29]	(29,36]	(36,87]	
		Unadjusted HR (95% CI)	ref	0.82 (0.64, 1.07)	1.07 (0.82, 1.39)	0.91 (0.70, 1.19)	1.00 (0.92, 1.09)
		Adjusted[a] HR (95% CI)	ref	0.76 (0.57, 1.01)	1.01 (0.76, 1.35)	0.81 (0.60, 1.09)	0.97 (0.88, 1.06)
	Obese: 30+ (n=1760, subcohort n=889)	Median	18	24	29	38	
		Ranges	[3,21]	(21,26]	(26,32]	(32,80]	
		Unadjusted HR (95% CI)	ref	1.03 (0.78, 1.35)	1.10 (0.84, 1.43)	1.16 (0.88, 1.53)	1.05 (0.96, 1.15)
		Adjusted[a] HR (95% CI)	ref	0.94 (0.70, 1.28)	1.13 (0.84, 1.53)	1.18 (0.87, 1.60)	1.07 (0.97, 1.18)
First principal component	Normal: 18.5-24.9 (n=2094, subcohort n=1105)	Median	-1	-0	1	2	
		Ranges	[-9.9,-0.588]	(-0.588,0.371]	(0.371,1.23]	(1.23,4.65]	
		Unadjusted HR (95% CI)	ref	1.25 (0.98, 1.60)	0.95 (0.74, 1.22)	1.16 (0.90, 1.48)	1.02 (0.94, 1.10)
		Adjusted[a] HR (95% CI)	ref	1.36 (1.04, 1.78)	0.92 (0.70, 1.20)	1.15 (0.88, 1.50)	1.00 (0.92, 1.09)
	Overweight: 25.0-29.9 (n=1839, subcohort n=942)	Median	-1	-0	1	2	
		Ranges	[-6.71,-0.75]	(-0.75,0.193]	(0.193,0.965]	(0.965,4.87]	
		Unadjusted HR (95% CI)	ref	0.84 (0.64, 1.10)	1.03 (0.79, 1.35)	0.96 (0.73, 1.25)	1.01 (0.93, 1.10)
		Adjusted[a] HR (95% CI)	ref	0.89 (0.66, 1.20)	0.98 (0.73, 1.31)	0.91 (0.68, 1.23)	0.98 (0.89, 1.08)
	Obese: 30+ (n=1760, subcohort n=889)	Median	-2	-1	0	1	
		Ranges	[-8.26,-1.02]	(-1.02,-0.098]	(-0.098,0.644]	(0.644,5.12]	
		Unadjusted HR (95% CI)	ref	1.21 (0.92, 1.59)	1.13 (0.86, 1.49)	1.26 (0.96, 1.66)	1.06 (0.97, 1.16)
		Adjusted[a] HR (95% CI)	ref	1.11 (0.82, 1.52)	1.16 (0.85, 1.58)	1.24 (0.91, 1.68)	1.07 (0.97, 1.18)

[a] Adjusted for baseline smoking, alcohol, education, HRT, age at menarche, age at first birth, oral contraceptive use, and menopause status.
[b] log transformed
[c] For first quartile compared to aggregate of upper three quartiles, the adjusted HR (95% CI) is 0.72 (0.56, 0.92) for iron and 0.84 (0.66, 1.09) for ferritin among women with a BMI $\geq$ 30 kg/m^2.
[d] Iron covariate in quartile units

Table S5: Breast cancer risk associated with increasing levels of iron-related biomarkers for women with premenopausal person-time.

	Quartile of iron-related biomarker				Linear trend over quartiles[d]
Biomarkers	Quartile 1[c]	Quartile 2	Quartile 3	Quartile 4	
Iron (μg/dL)					
Median	57	82	105	142	
n	451	462	449	431	
Ranges	[5,70]	(70,93]	(93,120]	(120,276]	
Unadjusted	ref	1.43 (1.03, 1.98)	1.38 (0.99, 1.93)	1.61 (1.16, 2.22)	1.15 (1.03, 1.27)
Adjusted[a]	ref	1.47 (1.01, 2.15)	1.35 (0.92, 1.98)	1.46 (0.99, 2.14)	1.10 (0.98, 1.24)
Ferritin[b] (μg/dL)					
Median	14	31	54	112	
n	463	441	444	445	
Ranges	[5,22]	(22,41]	(41,76]	(76,1625]	
Unadjusted	ref	1.42 (1.03, 1.95)	1.48 (1.07, 2.05)	1.07 (0.77, 1.48)	1.04 (0.94, 1.15)
Adjusted[a]	ref	1.48 (1.02, 2.14)	1.52 (1.05, 2.21)	1.14 (0.78, 1.66)	1.06 (0.95, 1.20)
Transferrin saturation (%)					
Median	17	25	32	44	
n	478	436	455	424	
Ranges	[2,21]	(21,28]	(28,37]	(37,90]	
Unadjusted	ref	1.50 (1.08, 2.08)	1.34 (0.97, 1.85)	1.33 (0.97, 1.84)	1.08 (0.98, 1.19)
Adjusted[a]	ref	1.72 (1.18, 2.50)	1.38 (0.95, 1.99)	1.20 (0.82, 1.75)	1.04 (0.92, 1.16)
First principal component					
Median	-1.6	-0.3	0.6	1.6	
n	449	448	448	448	
Ranges	[-7.96,-0.796]	(-0.796,0.201]	(0.201,1.02]	(1.02,4.85]	
Unadjusted	ref	1.51 (1.09, 2.10)	1.44 (1.03, 2.01)	1.55 (1.13, 2.14)	1.13 (1.02, 1.25)
Adjusted[a]	ref	1.68 (1.15, 2.45)	1.51 (1.03, 2.22)	1.48 (1.02, 2.15)	1.10 (0.98, 1.24)

[a] Adjusted for baseline smoking, alcohol, education, HRT, age at menarche, age at first birth, oral contraceptive use, and BMI.

[b] log transformed

[c] For first quartile compared to aggregate of upper three quartiles, the adjusted HR (95% CI) is 0.70 (0.51, 0.97) for iron, 0.73 (0.54, 0.99) for ferritin, 0.71 (0.52, 0.96) for transferrin saturation, and 0.64 (0.47, 0.88) for the first PC.

[d] Iron covariate in quartile units

Table S6: Breast cancer risk associated with increasing levels of iron-related biomarkers for participants who were postmenopausal at study entry

	Quartile of iron-related biomarker				Linear trend over quartiles[c]
Biomarkers	Quartile 1	Quartile 2	Quartile 3	Quartile 4	
Iron (μg/dL)					
Median	65	85	102	130	
n	958	948	917	932	
Ranges	[16,76]	(76,93]	(93,113]	(113,340]	
Unadjusted	ref	1.01 (0.84, 1.20)	0.99 (0.83, 1.19)	0.99 (0.83, 1.19)	1.00 (0.94, 1.05)
Adjusted[a]	ref	0.93 (0.77, 1.13)	0.98 (0.81, 1.20)	0.98 (0.80, 1.19)	1.00 (0.94, 1.06)
Ferritin[b] (μg/dL)					
Median	32	65	102	174	
n	966	929	938	922	
Ranges	[5,49]	(49,82]	(82,129]	(129,1404]	
Unadjusted	ref	1.19 (1.00, 1.43)	1.20 (1.00, 1.43)	1.15 (0.96, 1.38)	1.04 (0.99, 1.11)
Adjusted[a]	ref	1.10 (0.91, 1.34)	1.20 (0.99, 1.46)	1.10 (0.90, 1.33)	1.04 (0.98, 1.10)
Transferrin saturation (%)					
Median	20	26	33	42	
n	1004	992	935	824	
Ranges	[4,23]	(23,29]	(29,36]	(36,87]	
Unadjusted	ref	0.94 (0.79, 1.12)	1.06 (0.88, 1.26)	0.94 (0.78, 1.13)	0.99 (0.94, 1.05)
Adjusted[a]	ref	0.87 (0.72, 1.05)	1.03 (0.84, 1.25)	0.93 (0.76, 1.14)	1.00 (0.93, 1.06)
First principal component					
Median	-1.5	-0.3	0.5	1.5	
n	939	939	938	939	
Ranges	[-8.53,-0.808]	(-0.808,0.115]	(0.115,0.958]	(0.958,4.7]	
Unadjusted	ref	1.05 (0.88, 1.26)	1.02 (0.85, 1.22)	1.00 (0.83, 1.19)	1.00 (0.94, 1.05)
Adjusted[a]	ref	1.02 (0.84, 1.24)	1.01 (0.83, 1.23)	1.03 (0.84, 1.25)	1.01 (0.95, 1.07)

[a] Adjusted for baseline smoking, alcohol, education, HRT, age at menarche, age at first birth, oral contraceptive use, and BMI.

[b] log transformed

[c] Iron covariate in quartile units

Table S7: Breast cancer hazard ratios by menopause status at baseline and body iron status extreme thresholds

High/low indicator	Iron measure	Cut points for dichotomized iron measure thresholds	HR (95% CI)	n above/below threshold
Postmenopausal				
Low	Ferritin (μg / L)	$\leq$ 12	0.54 (0.37, 0.79)	107
		$\leq$ 25	0.82 (0.66, 1.02)	359
		$\leq$ 45	0.89 (0.77, 1.04)	873
	Transferrin saturation (%)	$\leq$ 20	1.03 (0.86, 1.23)	576
High	Ferritin (μg / L)	$\geq$ 300	1.03 (0.67, 1.59)	85
	Transferrin saturation (%)	$\geq$ 45	1.36 (1.07, 1.74)	278
		$\geq$ 50	1.31 (0.93, 1.85)	137
		$\geq$ 55	1.05 (0.66, 1.66)	72
		$\geq$ 60	1.24 (0.63, 2.47)	35
Premenopausal				
Low	Ferritin (μg / L)	$\leq$ 12	0.65 (0.45, 0.93)	166
		$\leq$ 25	0.88 (0.69, 1.12)	477
		$\leq$ 45	0.97 (0.77, 1.21)	864
	Transferrin saturation (%)	$\leq$ 20	0.76 (0.58, 1.00)	415
High	Ferritin (μg / L)	$\geq$ 200	0.93 (0.47, 1.84)	45
	Transferrin saturation (%)	$\geq$ 45	1.26 (0.88, 1.79)	200
		$\geq$ 50	1.10 (0.69, 1.74)	114
		$\geq$ 55	1.15 (0.62, 2.14)	60
		$\geq$ 60	1.64 (0.70, 3.84)	31

Table S8: Odds ratio (95% CI) of breast cancer subtypes* by iron biomarkers in case-only sample.

		Iron biomarkers			
Index group	counts	FE	FE sat	log(fertn)	PC1
One hormone receptor subtype (negative vs positive)					
ER-	ER+ (n= 2112);ER- (n= 379)	1.00 (0.99, 1.00)	0.99 (0.98, 1.00)	1.04 (0.91, 1.20)	0.97 (0.90, 1.05)
PR-	PR+ (n= 1739);PR- (n= 675)	1.00 (1.00, 1.01)	1.01 (0.99, 1.02)	1.04 (0.89, 1.23)	1.06 (0.97, 1.17)
HER2-	HER+ (n= 254);HER- (n= 1784)	1.00 (0.99, 1.00)	0.99 (0.99, 1.00)	1.06 (0.95, 1.18)	0.96 (0.90, 1.03)
Subtype combination (vs HR+/HER2-, n=1548)					
HR+/HER2+ or HR-/HER2+ vs HR+/HER2-	251	1.00 (0.99, 1.00)	0.99 (0.98, 1.00)	0.97 (0.82, 1.15)	0.93 (0.84, 1.02)
HR-/HER2- vs HR+/HER2-	213	1.00 (0.99, 1.00)	0.99 (0.97, 1.00)	1.10 (0.92, 1.31)	0.92 (0.83, 1.03)
Invasive vs In Situ					
	Invasive (n= 2169); InSitu (n= 607)	1.00 (1.00, 1.00)	1.00 (0.99, 1.01)	1.00 (0.90, 1.12)	1.02 (0.96, 1.09)

[*] Adjusted for age at diagnosis and menopause status at baseline.

Table S9: Odds ratio (95% CI) of breast cancer stage[a] by iron biomarkers in case-only sample.

		Iron biomarkers			
Stage (vs stage 0 (n=572))	n	Iron	Iron saturation	Ferritin[b]	PC1
I	1314	1.00 (1.00, 1.00)	1.00 (0.99, 1.01)	0.98 (0.87, 1.11)	0.97 (0.91, 1.05)
II	509	1.00 (0.99, 1.00)	0.99 (0.98, 1.00)	0.94 (0.81, 1.09)	0.91 (0.83, 0.99)
III	136	1.00 (0.99, 1.00)	0.99 (0.97, 1.01)	0.86 (0.69, 1.09)	0.89 (0.78, 1.02)
IV	20	1.00 (0.99, 1.02)	1.00 (0.96, 1.04)	1.24 (0.71, 2.18)	1.04 (0.75, 1.43)
X	22	0.99 (0.98, 1.01)	0.98 (0.94, 1.02)	0.87 (0.52, 1.47)	0.85 (0.62, 1.17)

[a] Adjusted for age at diagnosis and menopause status at baseline.
[b] log transformed

Supplemental text regarding sample handling and laboratory assessments

The Advanced Research and Diagnostic Laboratory at the University of Minnesota acted as the central laboratory for this study, receiving 7,621 serum samples in straws in a frozen state packaged on dry ice in goblets of 100 samples per goblet. Samples were stored frozen at -80C until testing. To prepare samples for analysis the straw samples were thawed to room temperature, then the straw was cut with a scissor and the sample expelled into a labelled cryovial and capped. Scissors were cleaned with an alcohol pad between each sample. Vials were mixed by inversion immediately before testing. Analysis was performed on the Roche Cobas 6000 Chemistry analyzer (Roche Diagnostics, Mannheim, Germany) using Roche reagents and calibrators. Test methodologies and inter-assay coefficient of variation were as follows. Iron is a colorimetric FerroZine end-point assay with an interassay CV of 2.5% at a concentration 77 ug/dL. Ferritin is particle enhanced immunoturbidimetric assay with an interassay CV of 2.8% at a concentration of 259 ug/L. Unsaturated Iron Binding Capacity (UIBC) is a colorimetric assay with an inter-assay CV of 3.3% at a concentration of 239 ug/dL. All samples had serum indices measurements for hemolysis, icterus and lipemia performed on the Roche Cobas 6000 analyzer by spectrophotometric method. Each assay has manufacture defined thresholds for each indice and results were not reported if this threshold was exceeded. Two levels of quality control were analyzed twice per day, once at the beginning of daily testing and once at the end. One quality control was a laboratory developed pooled serum sample and the other a Roche Precipath U commercially available product. Assay calibration was performed per manufacture specifications using manufacturer calibrators. Sample results were reported to the laboratory information system via electronic instrument interface only after quality control and calibration results were deemed acceptable per laboratory and manufacture standards.

Results that could not be reported were primarily due to sample hemolysis. Our Cobas analyzer is programmed to automatically perform specimen integrity checks for hemolysis, lipemia and icterus. The UIBC assay is particularly sensitive to hemolysis and has the lowest hemolysis index threshold for acceptability which is why more UIBC test results were not reported.