Table 1. Participating cohorts, sample collection and storage, and number and characteristics of cases and controls

Cohort[1]	Country	Source population	Years of blood draw	Sample type used in study	Storage temperature	Effective cohort size[2]	Cases/ Controls	Median age at blood donation in controls yr (min-max)	Median time to diagnosis, yr (min-max)
BGS [1]	UK	General population	2003-2010	Plasma	-180ºC	46,344	439/439	44.0 (21.0-57.0)	3.0 (0.0-9.0)
CLUE II [2, 3]	USA	Residents of Washington County, MD	1989	Plasma	-70ºC	2,899	136/136	40.0 (22.0-49.0)	13.5 (0.7-23.5)
CSB [4, 5]	USA	Attendees of breast cancer screening centers in Columbia, Missouri	1977-1987	Serum	-70ºC	2,459	101/101	44.6 (33.3-54.7)	16.6 (0.2-23.3)
Guernsey [6, 7]	UK	General population	1977-1990	Serum	-20ºC	3,120	176/176	40.1 (32.0-53.5)	16.7 (0.6-30.4)
NHS [8]	USA	Nurses	1989-1990	Plasma	-130ºC	6,926	136/136	46.7 (43.0-53.8)	4.6 (0.1-13.8)
NHSII [9, 10]	USA	Nurses	1996-1999	Plasma	-130ºC	22,000	395/395	42.8 (33.1-52.2)	4.9 (0.1-13.3)
NSMSC [11, 12]	Sweden	Attendees of a population-based screening program in Västerbotten	1995-2006	Plasma	-80ºC	3,569	66/66	49.5 (39.6-53.3)	6.1 (0.0-13.6)
NYUWHS [13, 14]	USA	Attendees of a breast cancer screening center, NYC	1985-1991	Serum	-80ºC	7,222	749/749	44.2 (34.3-56.5)	12.8 (0.6-24.5)
ORDET [15]	Italy	Residents in Varese Province	1987-1992	Serum	-80ºC	5,942	263/263	44.4 (35.2-54.1)	9.7 (0.3-19.2)
Sister Study [16]	USA	Sisters of women with breast cancer	2003-2009	Serum	-180ºC	14,772	374/661	46.5 (35.1-54.6)	2.8 (0.0-8.4)

[1] Cohort abbreviations: BGS: Breakthrough Generations Study; CLUE II: Campaign Against Cancer and Heart Disease; CSB: Columbia, Missouri Serum Bank; NHS: Nurses' Health Study; NHSII: Nurses' Health Study II; NSMSC: Northern Sweden Mammography Screening Cohort; NYUWHS: New York University Women's Health Study; ORDET: Hormones and Diet in the Etiology of Breast Cancer.

[2] Participants who would have been eligible if diagnosed with breast cancer during follow-up (i.e. female participants with blood collected prior to menopause).

Table 2. Baseline characteristics of cases and controls

Characteristic[1]	Cases (N = 2835) N (%)	Controls (N = 3122) N (%)	P-value[2]
Age at blood draw, years			Matched
<35	108 (3.8%)	111 (3.6%)	
35-39	534 (18.8%)	535 (17.1%)	
40-44	897 (31.6%)	999 (32.0%)	
45-49	966 (34.1%)	1117 (35.8%)	
50-54	318 (11.2%)	349 (11.2%)	
55+	12 (0.4%)	11 (0.4%)	
Race/ethnicity[1]			0.75
White	2562 (93.7%)	2800 (93.9%)	
Black/African American	118 (4.3%)	120 (4.0%)	
Other	53 (1.9%)	61 (2.0%)	
Education[1]			0.02
High school or less	759 (30.2%)	873 (30.8%)	
Some college/university, vocational training or more	1758 (69.8%)	1963 (69.2%)	
BMI[1], kg/m^2			0.04[3]
<18.5	51 (1.8%)	57 (1.8%)	
18.5-24.9	1702 (60.4%)	1779 (57.4%)	
25-29.9	710 (25.2%)	777 (25.0%)	
30+	353 (12.5%)	489 (15.8%)	
Age at menarche, years			0.44[3]
<12	603 (21.7%)	659 (21.6%)	
12	788 (28.3%)	803 (26.3%)	
13	786 (28.2%)	903 (29.5%)	
14+	606 (21.8%)	692 (22.6%)	
Parity[1]			0.05[3]
0	680 (24.6%)	710 (23.3%)	
1	400 (14.5%)	435 (14.3%)	
2	1028 (37.2%)	1138 (37.4%)	
3+	653 (23.7%)	758 (24.9%)	
Age at first full-term pregnancy[1], years			0.003[3]
<20	161 (7.5%)	226 (9.4%)	
21-24	696 (32.4%)	825 (34.4%)	
25-29	784 (36.5%)	834 (34.8%)	
≥30 or nulliparous	506 (23.6%)	515 (21.5%)	
Oral contraceptive use[1]			0.15
Never user	736 (26.9%)	772 (25.5%)	
Former user	1830 (66.9%)	2083 (68.8%)	
Current user	171 (6.2%)	174 (5.7%)	
Partial oophorectomy[1]			0.02
No	2747 (97.3%)	2989 (96.1%)	
Yes	76 (2.7%)	120 (3.9%)	
Family history of breast cancer[4]			<0.001
No	1984 (80.6%)	2143 (87.1%)	
Yes	477 (19.4%)	318 (12.9%)	
Benign breast biopsy[1]			<0.001
No	2096 (75.8%)	2511 (82.3%)	
Yes	669 (24.2%)	541 (17.7%)	
Smoking status[1]			0.02
Never	1576 (58.8%)	1847 (62.5%)	
Former	752 (28.1%)	751 (25.4%)	
Current	352 (13.1%)	359 (12.1%)	

[1] Missing data: race/ethnicity: 4.1%; education: 10.1%; BMI: 0.7%; age at menarche: 2.0%; parity: 2.6%; age at first full-term pregnancy: 0.2%; oral contraceptive use: 3.2%; partial oophorectomy: 0.4%; benign breast biopsy: 2.4%; smoking status: 5.4%.

[2] p-value from conditional logistic regression model

[3] p for trend from conditional logistic regression model for ordered categorical variable

[4] Calculated after excluding the Sister Study (all participants in this study have a family history of breast cancer).

Table 3. AMH assay, lowest detected value (LDV) and AMH geometric means (95% CIs) for cases and controls

Cohort[1]	Assay[2]	LDV[3], pmol/l	< LDV, %		Geometric mean[4] (95% CI), pmol/l		Age-adjusted geometric mean[4] (95% CI), pmol/l	
			Cases	Controls	Cases	Controls	Cases	Controls
BGS	picoAMH ELISA	0.0165	4.1	5.9	2.57 (2.12, 3.11)	2.33 (1.91, 2.86)	2.31 (2.00,2.67)	1.95 (1.68,2.27)
CLUE II	picoAMH ELISA	0.0165	3.7	2.9	4.71 (3.29, 6.75)	4.14 (2.91, 5.90)	1.85 (1.41,2.42)	1.52 (1.14,2.01)
CSB	picoAMH ELISA	0.0330	5.0	12.9	2.52 (1.67, 3.81)	1.39 (0.91, 2.13)	2.90 (2.15,3.92)	1.61 (1.17,2.20)
Guernsey	picoAMH ELISA	0.0264	5.7	2.8	3.12 (2.33, 4.17)	3.68 (2.84, 4.78)	1.29 (1.03,1.63)	1.36 (1.07,1.73)
NHS	picoAMH ELISA	0.0165	4.4	10.3	2.03 (1.45, 2.83)	1.03 (0.71, 1.52)	4.21 (3.24,5.46)	2.22 (1.69,2.92)
NHSII	picoAMH ELISA	0.0165	1.5	1.5	6.77 (5.83, 7.87)	5.21 (4.47, 6.06)	4.55 (3.90,5.30)	3.15 (2.68,3.70)
NSMSC	picoAMH ELISA	0.0165	6.1	7.6	1.00 (0.58, 1.70)	0.71 (0.43, 1.18)	2.98 (2.05,4.33)	2.23 (1.51,3.31)
NYUWHS	picoAMH ELISA	0.143	15.4	15.6	2.54 (2.21, 2.92)	2.32 (2.02, 2.67)	2.76 (2.47,3.08)	2.40 (2.14,2.70)
ORDET	picoAMH ELISA	0.0264	3.8	9.5	2.84 (2.25, 3.58)	1.93 (1.48, 2.51)	2.79 (2.31,3.36)	1.93 (1.59,2.34)
Sister Study	Ultrasensitive & picoAMH ELISA[5]	0.0214	16.0	18.5	1.20 (0.93, 1.54)	1.03 (0.85, 1.25)	2.30 (1.96,2.70)	1.80 (1.59,2.05)

[1] Cohort abbreviations: BGS: Breakthrough Generations Study; CLUE II: Campaign Against Cancer and Heart Disease; CSB: Columbia, Missouri Serum Bank; NHS: Nurses' Health Study; NHSII: Nurses' Health Study II; NSMSC: Northern Sweden Mammography Screening Cohort; NYUWHS: New York University Women's Health Study; ORDET: Hormones and Diet in the Etiology of Breast Cancer.

[2] Assays were conducted at Ansh Labs, except for the NYUWHS (Core Laboratory, Massachusetts General Hospital Pathology Service) and the Sister Study (Reproductive Endocrinology Laboratory, University of Southern California).

[3] LDV varied depending on the dilution factor used.

[4] Subjects with AMH measurement below the LDV were assigned the value of LDV divided by the square root of 2. Age-adjusted means adjusted for age and age-squared. Samples with AMH above the highest detectable value (n=14 total, 3 from CLUE II and 11 from NYUWHS) were set to the highest detectable value.

[5] All samples were measured using the Ultrasensitive assay; samples with AMH concentration < the LDV of the ultrasensitive assay (0.500 pmol/l) were re-measured using the picoAMH ELISA assay.

Table 4. Odds ratios (ORs) and 95% confidence intervals (95% CIs) for breast cancer associated with AMH concentration

| | AMH quartiles[1] | | | | P_{trend}[5] |
	Q1	Q2	Q3	Q4	
Cases/Controls	631/789	684/777	711/779	809/777	.
Unadjusted OR[2] (95% CI)	1.00 (Referent)	1.20 (1.02, 1.41)	1.35 (1.14, 1.61)	1.64 (1.35, 1.98)	<.0001
Adjusted OR[3] (95% CI)	1.00 (Referent)	1.18 (1.00, 1.39)	1.32 (1.10, 1.58)	1.60 (1.31, 1.94)	<.0001
Adjusted OR[3] (95% CI), among women with testosterone measurements	1.00 (Referent)	1.18 (0.99, 1.40)	1.34 (1.11, 1.61)	1.62 (1.32, 1.98)	<.0001
Adjusted OR[4] (95% CI), including adjustment for testosterone	1.00 (Referent)	1.17 (0.99, 1.40)	1.33 (1.10, 1.60)	1.58 (1.29, 1.93)	<.0001

[1] Defined using cohort-specific cutpoints.

[2] Estimated using conditional logistic regression (cohort and age are adjusted for through matching).

[3] Estimated using conditional logistic regression and adjusting for race/ethnicity (white, black, other or unknown), education (high school or less, some college or higher, unknown), BMI (ordered categorical, <18.5, 18.5-25, 25-30, 30+ kg/m^2), age at menarche (ordered categorical, <12, 12, 13, 14+ years), parity (ordered categorical, 0, 1, 2, 3+), age at 1st FTP (ordered categorical, <=20, 21-25, 26-30, 30+ years or nulliparous), oral contraceptive use (never, former, current, unknown), partial oophorectomy (no, yes, unknown), family history of breast cancer (no, yes), benign breast biopsy (no, yes, unknown), and smoking status (never, former, current, unknown).

[4] Estimated using conditional logistic regression and adjusting for variables in footnote 2 and testosterone (cohort-specific quartiles, with measurements from previous studies calibrated to the Mayo LC-MS/MS assay).

[5] P_{trend} was calculated using ordered-categorical AMH.

Table 5. Odds ratios[1] (ORs) and 95% confidence intervals (95% CIs) for breast cancer associated with AMH concentration by tumor characteristics

		AMH quartiles[2]				P_{trend}[3]	$P_{interaction}$[4]
		Q1	Q2	Q3	Q4		
Invasiveness							0.41
Invasive	Cases/Controls	508/636	547/619	564/595	636/606		
	Adjusted OR (95% CI)	1.00 (Referent)	1.19 (0.99, 1.43)	1.39 (1.14, 1.70)	1.67 (1.34, 2.09)	<.0001	
In situ	Cases/Controls	122/153	136/156	147/184	172/169		
	Adjusted OR (95% CI)	1.00 (Referent)	1.19 (0.79, 1.79)	1.10 (0.72, 1.69)	1.35 (0.85, 2.13)	0.25	
ER status							0.21
ER+	Cases/Controls	324/438	353/424	377/411	441/439		
	Adjusted OR (95% CI)	1.00 (Referent)	1.27 (1.01, 1.60)	1.52 (1.19, 1.96)	1.74 (1.33, 2.28)	<.0001	
ER-	Cases/Controls	84/90	93/108	91/109	112/110		
	Adjusted OR (95% CI)	1.00 (Referent)	0.95 (0.60, 1.52)	1.02 (0.62, 1.69)	1.17 (0.68, 2.01)	0.54	
PR status							0.02
PR+	Cases/Controls	266/374	304/372	334/369	405/390		
	Adjusted OR (95% CI)	1.00 (Referent)	1.29 (1.00, 1.65)	1.61 (1.23, 2.11)	1.97 (1.48, 2.64)	<.0001	
PR-	Cases/Controls	142/154	142/160	134/151	148/159		
	Adjusted OR (95% CI)	1.00 (Referent)	0.96 (0.67, 1.39)	0.99 (0.66, 1.49)	1.00 (0.65, 1.55)	0.95	
HER2 status							0.37
HER2+	Cases/Controls	44/60	44/55	38/62	80/57		
	Adjusted OR (95% CI)	1.00 (Referent)	1.11 (0.58, 2.11)	1.17 (0.57, 2.44)	3.39 (1.55, 7.42)	0.002	
HER2-	Cases/Controls	182/275	227/280	244/263	266/279	.	
	Adjusted OR (95% CI)	1.00 (Referent)	1.36 (1.01, 1.83)	1.80 (1.31, 2.48)	2.05 (1.45, 2.92)	<.0001	
Joint receptor status							
ER+/PR+	Cases/Controls	259/360	288/358	317/354	386/371		0.15
	Adjusted OR (95% CI)	1.00 (Referent)	1.26 (0.97, 1.62)	1.58 (1.20, 2.08)	1.96 (1.46, 2.64)	<.0001	
ER+/PR-	Cases/Controls	65/78	65/66	60/57	55/68		
	Adjusted OR (95% CI)	1.00 (Referent)	1.25 (0.68, 2.28)	1.13 (0.58, 2.19)	0.82 (0.40, 1.68)	0.51	
ER-/PR+	Cases/Controls	7/14	16/14	17/15	19/19		
	Adjusted OR (95% CI)	1.00 (Referent)	3.10 (0.60, 15.9)	3.53 (0.60, 20.8)	3.23 (0.48, 21.9)	0.26	
ER-/PR-	Cases/Controls	77/76	77/94	74/94	93/91		
	Adjusted OR (95% CI)	1.00 (Referent)	0.83 (0.50, 1.39)	0.90 (0.51, 1.58)	1.15 (0.63, 2.09)	0.60	
Triple-negative (ER-/PR-/HER2-) tumors							
	Cases/Controls	29/28	25/35	28/29	33/42		
	Adjusted OR (95% CI)	1.00 (Referent)	0.84 (0.31, 2.28)	1.17 (0.41, 3.37)	1.02 (0.34, 3.04)	0.95	

[1] Estimated using conditional logistic regression model and adjusting for race/ethnicity (white, black, other or unknown), education (high school or less, some college or higher, unknown), BMI (<18.5, 18.5-25, 25-30, 30+ kg/m^2), age at menarche (ordered categorical, <12, 12, 13, 14+ years), parity (ordered categorical, 0, 1, 2, 3+), age at 1st FTP

(ordered categorical, <=20, 21-25, 26-30, 30+ years or nulliparous), oral contraceptive use (never, former, current, unknown), partial oophorectomy (no, yes, unknown), family history of breast cancer (no, yes), benign breast biopsy (no, yes, unknown), and smoking status (never, former, current, unknown).

[2] Defined using cohort-specific cutpoints.

[3] P_{trend} was calculated using ordered categorical AMH.

[4] $P_{interaction}$ was calculated by including an interaction term between AMH (ordered categorical) and each tumor characteristic.

Table 6. Odds ratios (ORs) and 95% confidence intervals (95% CIs) for breast cancer associated with AMH concentration by menopausal status at diagnosis

	AMH quartiles[1]				P_{trend}[4]	$P_{interaction}$[5]
	Q1	Q2	Q3	Q4		
Matched sets with both case and control(s) pre-menopausal at diagnosis/index date						0.34
Cases/Controls	222/292	282/339	327/369	369/374		
Adjusted OR[2] (95% CI)	1.00 (Referent)	1.21 (0.93, 1.56)	1.17 (0.91, 1.50)	1.35 (1.05, 1.73)	0.03	
Matched sets with both case and control(s) post-menopausal at diagnosis/index date						
Cases/Controls	161/176	90/116	96/94	100/75		
Adjusted OR[2] (95% CI)	1.00 (Referent)	0.88 (0.60, 1.30)	1.14 (0.74, 1.76)	1.61 (1.03, 2.53)	0.03	
Adjusted OR[3] (95% CI)	1.00 (Referent)	0.88 (0.59, 1.30)	1.13 (0.72, 1.79)	1.59 (0.96, 2.63)	0.06	

[1] Defined using cohort- and age-specific cutpoints.

[2] Estimated using conditional logistic regression model, adjusting for race/ethnicity (white, black, other or unknown), education (high school or less, some college or higher, unknown), BMI (<18.5, 18.5-25, 25-30, 30+ kg/m^2), age at menarche (ordered categorical, <12, 12, 13, 14+ years), parity (ordered categorical, 0, 1, 2, 3+), age at 1st FTP (ordered categorical, <=20, 21-25, 26-30, 30+ years or nulliparous), oral contraceptive use (never, former, current, unknown), partial oophorectomy (no, yes, unknown), family history of breast cancer (no, yes), benign breast biopsy (no, yes, unknown), and smoking status (never, former, current, unknown). Analyses were performed among women with known age at menopause.

[3] Estimated using conditional logistic regression model and adjusting for variables in footnote 2 and age at menopause.

[4] P_{trend} was calculated using ordered categorical AMH.

[5] $P_{interaction}$ was calculated by including an interaction term between AMH (ordered categorical) and menopausal status at diagnosis.

Figure Legend:

Figure 1. Cohort-specific associations between AMH and breast cancer risk (ORs and 95% CIs for the 4th quartile vs. 1st quartile)[1]

References

1. Swerdlow AJ, Jones ME, Schoemaker MJ, Hemming J, Thomas D, Williamson J, Ashworth A. The Breakthrough Generations Study: design of a long-term UK cohort study to investigate breast cancer aetiology. *Br J Cancer* 2011;**105**: 911-7.

2. Helzlsouer KJ, Alberg AJ, Huang H-Y, Hoffman SC, Strickland PT, Brock JW, Burse VW, Needham LL, Bell DA, Lavigne JA. Serum concentrations of organochlorine compounds and the subsequent development of breast cancer. *Cancer Epidemiology Biomarkers & Prevention* 1999;**8**: 525-32.

3. Visvanathan K, Crum RM, Strickland PT, You X, Ruczinski I, Berndt SI, Alberg AJ, Hoffman SC, Comstock GW, Bell DA, Helzlsouer KJ. Alcohol dehydrogenase genetic polymorphisms, low-to-moderate alcohol consumption, and risk of breast cancer. *Alcohol Clin Exp Res* 2007;**31**: 467-76.

4. Dorgan J, Stanczyk F, Egleston B, Kahle L, Shaw C, Spittle C, Godwin A, Brinton L. Prospective case-control study of serum mullerian inhibiting substance and breast cancer risk. *J Natl Cancer Inst* 2009;**101**: 1501 - 9.

5. Dorgan JF, Stanczyk FZ, Kahle LL, Brinton LA. Prospective case-control study of premenopausal serum estradiol and testosterone levels and breast cancer risk. *Breast Cancer Res* 2010;**12**: R98.

6. Fentiman I, Hanby A, Allen D, Key T, Meilahn E. Hormone dependency of breast tumours developing in the Guernsey Cohort Study. *Breast cancer research and treatment* 2006;**97**: 205-8.

7. Thomas HV, Key TJ, Allen DS, Moore JW, Dowsett M, Fentiman IS, Wang DY. A prospective study of endogenous serum hormone concentrations and breast cancer risk in premenopausal women on the island of Guernsey. *Br J Cancer* 1997;**75**: 1075-9.

8. Eliassen AH, Missmer SA, Tworoger SS, Spiegelman D, Barbieri RL, Dowsett M, Hankinson SE. Endogenous steroid hormone concentrations and risk of breast cancer among premenopausal women. *Journal of the National Cancer Institute* 2006;**98**: 1406-15.

9. Eliassen AH, Zeleniuch-Jacquotte A, Rosner B, Hankinson SE. Plasma anti-Mullerian hormone concentrations and risk of breast cancer among premenopausal women in the Nurses' Health Studies. *Cancer Epidemiol Biomarkers Prev* 2016.

10. Fortner RT, Eliassen AH, Spiegelman D, Willett WC, Barbieri RL, Hankinson SE. Premenopausal endogenous steroid hormones and breast cancer risk: results from the Nurses' Health Study II. *Breast Cancer Res* 2013;**15**: R19.

11. Scarmo S, Afanasyeva Y, Lenner P, Koenig KL, Horst RL, Clendenen TV, Arslan AA, Chen Y, Hallmans G, Lundin E, Rinaldi S, Toniolo P, Shore RE, Zeleniuch-Jacquotte A. Circulating levels of 25-hydroxyvitamin D and risk of breast cancer: a nested case-control study. *Breast Cancer Res* 2013;**15**: R15.

12. Lukanova A, Lundin E, Zeleniuch-Jacquotte A, Muti P, Mure A, Rinaldi S, Dossus L, Micheli A, Arslan A, Lenner P, Shore RE, Krogh V, Koenig KL, Riboli E, Berrino F, Hallmans G, Stattin P, Toniolo P, Kaaks R. Body mass index, circulating levels of sex-steroid hormones, IGF-I and IGF-binding protein-3: a cross-sectional study in healthy women. *Eur J Endocrinol* 2004;**150**: 161-71.

13. Toniolo PG, Pasternack BS, Shore RE, Sonnenschein E, Koenig KL, Rosenberg C, Strax P, Strax S. Endogenous hormones and breast cancer: a prospective cohort study. *Breast cancer research and treatment* 1991;**18**: S23-S6.

14. Zeleniuch-Jacquotte A, Afanasyeva Y, Kaaks R, Rinaldi S, Scarmo S, Liu M, Arslan AA, Toniolo P, Shore RE, Koenig KL. Premenopausal serum androgens and breast cancer risk: a nested case-control study. *Breast Cancer Res* 2012;**14**: R32.

15. Micheli A, Muti P, Secreto G, Krogh V, Meneghini E, Venturelli E, Sieri S, Pala V, Berrino F. Endogenous sex hormones and subsequent breast cancer in premenopausal women. *Int J Cancer* 2004;**112**: 312-8.

16. Nichols HB, Baird DD, Stanczyk FZ, Steiner AZ, Troester MA, Whitworth KW, Sandler DP. Anti-Mullerian Hormone Concentrations in Premenopausal Women and Breast Cancer Risk. *Cancer prevention research (Philadelphia, Pa)* 2015.