S Table 1: Description of the BCAC studies

Abbreviation	Study	Country	Case ascertainment	Breast cancer case definition	Age	Ref
ABCFS	Australian Breast Cancer Family Study	Australia	Population-based case-control study	All cases diagnosed < age 40 plus a random sample of those diagnosed ages 40-59 from cancer registries in Victoria and New South Wales, plus a limited number diagnosed aged 60-69; cases living in Melbourne recruited from 1992-99 and in Sydney from 1993-98.	23-69	(1)
BREOGAN	Breast Oncology Galicia Network	Spain	Population-based case-control	A population-based study conducted since 2004 in two cities in Galicia, Spain (Vigo and Santiago) covering approx.700,000 inhabitants. The study currently includes 1000 breast cancer cases with blood plus risk factor questionnaire.	20-85	(2;3)
CGPS	Copenhagen General Population Study	Denmark	Population-based	Consecutive, incident cases from 1 hospital with centralized care for a population of 400,000 women from 2001 to the present.	26-100	(4;5)
GESBC	Genetic Epidemiology Study of Breast Cancer by Age 50	Germany	Population-based study of women <50 years	All incident cases diagnosed <50 years of age in 1992-5 in two regions: Rhein-Neckar-Odenwald and Freiburg, by surveying the 38 clinics serving these regions	24-50	(6)
HEBCS	Helsinki Breast Cancer Study	Finland	Hospital-based	(1) Consecutive cases (883) from the Department of Oncology, Helsinki University Central Hospital 1997-8 and 2000, (2) Consecutive cases (986) from the Department of Surgery, Helsinki University Central Hospital 2001 – 2004, (3) Familial breast cancer patients (536) from the Helsinki University Central Hospital, Departments of Oncology and Clinical Genetics (1995-)	22-96	(7-9)
HERPACC	Hospital-based Epidemiologic Research Program at Aichi Cancer Center	Japan	Hospital-based case-controls study	Incident breast cancer cases who firstly visited Aichi Cancer Center between 2001 and 2005 and were diagnosed within 1 year from the first visit. No previous history of any type of cancer.	23-79	(10)
NC-BCFR	Northern California Breast Cancer Family Registry	USA	Population-based familial case-control study	Cases included those enrolled in the NC-BCFR as part of Phase I and II recruitment. Incident cases aged <65 years diagnosed between 1995 and 2003 were identified through the SEER cancer registry of the Greater San Francisco Bay Area. All cases likely at increased genetic risk were eligible to enroll in the BCFR (dx at age <35 yrs, personal history of ovarian or childhood cancer, bilateral breast cancer with 1st dx at age <50, family history of breast or ovarian cancer in first-degree relatives). Cases not meeting these criteria were randomly sampled (2.5% of whites, 30% of African Americans, 28% of Hispanics, 38% of Asian Americans).	22-64	(11)
PBCS	NCI Polish Breast Cancer Study	Poland	Population-based	Incident cases from 2000-3 identified through a rapid identification system in participating hospitals covering ~ 90% of all eligible cases; periodic check against the cancer registries in Warsaw and Łódź to assure complete identification of cases	27-75	(12)
UCIBCS	UCI Breast Cancer Study	USA	Population-based case-control study	All cases diagnosed in Orange County, California, during one-year period beginning March 1, 1994. Ascertained through the population-based Cancer Surveillance Program of Orange County California (CSPOC)	24-90	(13;14)

S Table 2: Characteristics of the SEARCH study by post-diagnosis alcohol consumption

	Alcohol consumption (units/week)										
Characteristic	Non-drinkers	%	<=7	%	>7-<=14	%	>14	%	Total	%	P value*
N	2,329	28	3,996	47	1,454	17	667	8	8,446		
Age											
Mean	45		53		53		53		54		<0.0001
Range	23-71		23-73		25-69		30-69		23-73		
Menopausal status											<0.0001
Premenopausal	350	15	691	17	233	16	114	17	1,388	16	
Perimenopausal	833	36	1,529	38	627	43	296	44	3,285	39	
Postmenopausal	1,146	49	1,776	44	594	41	257	39	3,773	45	
Stage											<0.0001
I	987	48	1,744	49	692	52	326	55	3,749	50	
II	954	46	1,637	46	575	44	241	41	3,407	45	
III	82	4	140	4	45	3	22	4	289	4	
IV	34	2	39	1	8	1	3	1	84	1	
Missing	272	12	436	11	134	9	75	11	917	11	
Grade											0.07
I	397	21	689	21	300	24	129	24	1,515	22	
II	939	50	1,618	49	587	47	269	50	3,413	49	
III	548	29	1,003	30	352	28	143	26	2,046	29	
Missing	445	19	686	17	215	15	126	19	1,472	17	
BMI											<0.0001
<=22.7	425	19	903	23	354	25	187	29	1,869	23	
22.8-25.2	459	20	1,047	27	417	29	187	29	2,110	25	
25.3-28.4	532	23	970	25	371	26	164	25	2,037	25	
28.5+	849	37	1,006	26	289	20	118	18	2,262	27	
Missing	64	3	70	2	23	2	11	2	168	2	
ER status											0.03
Negative	321	20	529	19	187	18	74	16	1,111	19	
Positive	1,273	80	2,300	81	861	82	396	84	4,830	81	
Missing	735	32	1,167	29	406	28	197	30	2,505	30	
Smoking											<0.0001
Non-smoker	1,289	55	2,333	58	636	44	212	32	4,470	53	
Former smoker	637	27	1,153	29	569	39	286	43	2,645	31	
Current smoker	400	17	506	13	248	17	168	25	1,322	16	
Missing	3	0	4	0	1	0	1	0	9	0	
Socioeconomic status											<0.0001
1 (least deprived)	389	17	838	21	329	23	130	20	1,686	20	
2	404	17	841	21	317	22	124	19	1,686	20	
3	443	19	794	20	299	21	147	22	1,683	20	
4	494	21	766	19	282	19	145	22	1,687	20	
5	596	26	745	19	224	15	118	18	1,683	20	
Missing	3	0	12	0	3	0	3	0	21	0	

*From ordinal logistic regression

S Table 3: Characteristics of the EPIC study by pre-diagnosis alcohol consumption

	Alcohol consumption (units/week)										
Characteristic	Non-drinkers	%	<=7	%	>7-<=14	%	>14	%	Total	%	P value*
N	1,492	14	5,088	48	1,949	19	2,032	19	10,561	100	
Age											0.12
Mean	60		59		60		60		60		
Range	31-85		25-93		28-92		28-88		25-93		
Menopausal status											
Premenopausal	53	4	195	4	67	3	43	2	358	3	<0.0001
Perimenopausal	399	27	1,432	28	498	26	503	25	2,832	27	
Postmenopausal	1,040	70	3,461	68	1384	71	1,486	73	7,371	70	
Stage											0.45
I	668	55	2,109	55	812	56	914	55	4,503	55	
II	414	34	1,423	37	497	35	604	36	2,938	36	
III	110	9	253	7	99	7	120	7	582	7	
IV	24	2	71	2	30	2	29	2	154	2	
Missing	276	19	1,232	24	511	26	365	18	2,384	23	
Grade											0.02
I	176	19	494	19	186	20	170	17	1,026	19	
II	407	45	1,158	45	372	41	418	42	2,355	44	
III	322	36	935	36	351	39	404	41	2,012	37	
Missing	587	39	2,501	49	1040	53	1,040	51	5,168	49	
BMI											<0.0001
<=22.7	404	27	1,717	34	744	38	795	39	3,660	35	
22.8-25.2	342	23	1,359	27	539	28	570	28	2,810	27	
25.3-28.4	350	23	1,057	21	397	20	424	21	2,228	21	
28.5+	396	27	955	19	269	14	243	12	1,863	18	
ER status											0.34
Negative	175	18	739	22	240	18	281	19	1,435	20	
Positive	807	82	2,674	78	1066	82	1,206	81	5,753	80	
Missing	510	34	1,675	33	643	33	545	27	3,373	32	
Smoking status											<0.0001
Non-smoker	945	65	2,872	58	1015	53	859	43	5,691	55	
Former smoker	253	17	1,219	25	508	27	587	30	2,567	25	
Current smoker	254	17	860	17	378	20	530	27	2,022	20	
Missing	40	3	137	3	48	2	56	3	281	3	
Socioeconomic status											<0.0001
1 (most educated)	215	15	1,088	23	525	28	642	33	2,470	24	
2	334	23	1,226	26	490	26	538	27	2,588	26	
3	249	17	1,209	25	455	24	407	21	2,320	23	
4	527	36	1,177	25	393	21	350	18	2,447	24	
5	120	8	94	2	23	1	32	2	269	3	
Missing	47	3	294	6	63	3	63	3	467	4	

*From ordinal logistic regression

S Table 4: Distribution of alcohol consumption by country in the EPIC cohort

Country	Non-drinkers	%	<=7	%	>7-<=14	%	>14	%	Total
Denmark	30	2	510	39	328	25	438	34	1,306
France	346	13	1,150	42	551	20	698	25	2,745
Germany	36	5	433	55	145	19	168	21	782
Greece	61	32	106	55	14	7	12	6	193
Italy	216	22	378	39	188	19	195	20	977
Netherlands	145	17	362	43	145	17	195	23	847
Norway	178	20	617	70	85	10	3	0	883
Spain	222	49	152	33	38	8	44	10	456
Sweden	159	15	599	58	174	17	104	10	1,036
UK	99	7	781	58	281	21	175	13	1,336
Total	1,492	14	5,088	48	1,949	18	2,032	19	10,561

S Table 5: Characteristics of the BCAC studies

Characteristic	ABCFS	BREOGAN	CGPS	GESBC	HEBCS	HERPACC	NC-BCFR	PBCS	UCIBCS	Total
N	1,336	1,192	2,574	612	1,288	453	1,418	571	788	10,232
Mortality										
All-cause	394	58	424	205	228	68	235	71	228	1,911
Breast cancer	321	0	24	153	116	31	103	22	90	860
Alcohol intake (units/week)										
Non-drinkers	692	568	588	158	110	299	852	2	184	3,453
<=7	228	145	798	270	1,167	94	390	451	385	3,928
>7-<=14	216	260	515	82	11	32	80	80	142	1,418
14+	200	219	673	102	0	28	96	38	77	1,433
Age (year)										
Mean	43	56	61	43	57	52	51	53	58	54
Range	23-69	28-88	24-93	20-51	25-95	23-78	21-78	27-75	18-90	18-95
Menopausal status										
Premenopausal	787	217	283	348	163	105	344	100	119	2,466
Perimenopausal	369	339	520	264	403	161	519	238	225	3,038
Postmenopausal	180	632	1,771	0	722	187	555	233	444	4,724
ER status										
Negative	400	206	362	193	207	113	295	169	131	2,076
Positive	782	906	1,762	328	1,053	308	842	356	499	6,836
Missing	154	80	450	91	28	32	281	46	158	1,320
Stage										
I	0	0	1,246	228	813	155	422	239	512	3,615
II	0	0	820	278	383	191	399	218	215	2,504
III	0	0	70	56	37	69	47	26	19	324
IV	0	0	0	20	39	20	19	6	14	118
Missing	1,336	1,192	438	30	16	18	531	82	28	3,671
Grade										
I	0	195	565	37	352	43	209	126	104	1,631
II	0	543	1,008	276	563	108	491	262	296	3,547
III	0	293	398	224	342	57	438	122	232	2,106
Missing	1,336	161	603	75	31	245	280	61	156	2,948

S Table 6: Association of alcohol consumption and mortality

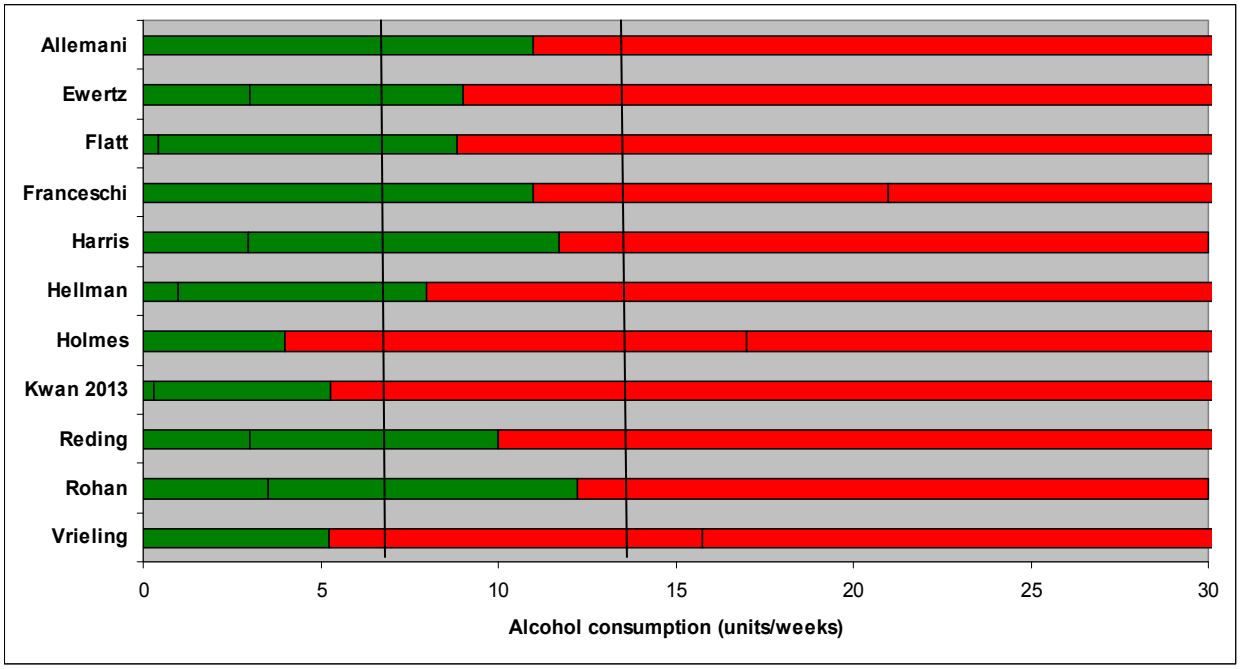
Study	Drinking category (units/week)	N	Uni-variate All-cause mortality Events	HR	LCL	UCL	Uni-variate Breast cancer specific mortality Events	HR	LCL	UCL	Mutlti-variate* All-cause mortality Events	HR	LCL	UCL	Mutlti-variate* Breast cancer specific mortality Events	HR	LCL	UCL
SEARCH	Linear estimates	8,446	1,506	0.88	0.83	0.93	1,213	0.90	0.84	0.96	945	0.90	0.83	0.98	765	0.93	0.85	1.01
	0	2,329	456				353				277				212			
	<=7	3,996	726	0.89	0.80	1.01	596	0.94	0.83	1.08	469	0.95	0.82	1.11	394	1.04	0.88	1.23
	>7-<=14	1,454	221	0.71	0.61	0.84	177	0.74	0.61	0.88	139	0.78	0.63	0.96	109	0.81	0.64	1.03
	>14	667	103	0.74	0.60	0.92	87	0.81	0.64	1.02	60	0.77	0.58	1.03	50	0.86	0.63	1.18
EPIC	Linear estimates	10,561	1,422	0.94	0.89	1.00	749	0.91	0.84	0.99	395	0.98	0.88	1.09	174	1.06	0.90	1.24
	0	1,492	227				132				68				35			
	<=7	5,088	694	0.84	0.72	0.98	371	0.80	0.65	0.99	187	0.99	0.74	1.33	82	1.03	0.67	1.58
	>7-<=14	1,949	229	0.71	0.59	0.86	111	0.63	0.48	0.82	58	0.88	0.61	1.26	23	0.95	0.55	1.64
	>14	2,032	272	0.84	0.69	1.01	135	0.78	0.60	1.00	82	0.97	0.69	1.37	34	1.23	0.74	2.03
BCAC	Linear estimates	10,232	1,911	0.91	0.87	0.96	860	0.95	0.89	1.02	963	0.88	0.82	0.95	355	0.94	0.83	1.07
	0	3,453	726				352				303				108			
	<=7	3,928	680	0.71	0.63	0.80	307	0.79	0.66	0.94	434	0.62	0.53	0.73	181	0.67	0.51	0.88
	>7-<=14	1,418	259	0.83	0.71	0.96	104	0.89	0.71	1.11	112	0.73	0.59	0.92	32	0.91	0.61	1.36
	>14	1,433	246	0.76	0.65	0.88	97	0.87	0.69	1.10	114	0.70	0.56	0.87	34	0.85	0.57	1.27

* Both EPIC and SEARCH were adjusted for stage, grade, ER status, BMI, smoking status, SES and menopausal status (EPIC estimates were also adjusted for country). BCAC adjusted for stage, grade, ER status, menopausal status and study.

S Table 7: Association of alcohol consumption and mortality in patients with stage I and II tumours compared to all patients in SEARCH

			All-cause				BCSS				All-cause				BCSS			
	Drinking Category	N	Events	HR	LCL	UCL	Events	HR	LCL	UCL	Events	HR	LCL	UCL	Events	HR	LCL	UCL
Stage1&2	Linear estimates	7,156	1228	0.89	0.83	0.95	974	0.92	0.86	0.99	832	0.91	0.84	0.99	660	0.95	0.87	1.04
	0	1,941	358	1.00	Ref		268	1.00	Ref		235	1.00	Ref		173	1.00	Ref	
	<=7	3,381	604	0.95	0.83	1.08	489	1.02	0.88	1.18	418	0.96	0.82	1.13	346	1.06	0.88	1.28
	>7-<=14	1,267	181	0.73	0.61	0.87	144	0.77	0.63	0.95	122	0.76	0.61	0.95	93	0.80	0.62	1.03
	14+	567	85	0.77	0.61	0.98	73	0.88	0.68	1.15	57	0.86	0.64	1.15	48	1.00	0.73	1.39
All cases	Linear estimates	8,446	1,506	0.88	0.83	0.93	1,213	0.90	0.84	0.96	945	0.90	0.83	0.98	765	0.93	0.85	1.01
	0	2,329	456	1.00	Ref		353	1.00	Ref		277	1.00	Ref		212	1.00	Ref	
	<=7	3,996	726	0.89	0.80	1.01	596	0.94	0.83	1.08	469	0.95	0.82	1.11	394	1.04	0.88	1.23
	>7-<=14	1,454	221	0.71	0.61	0.84	177	0.74	0.61	0.88	139	0.78	0.63	0.96	109	0.81	0.64	1.03
	14+	667	103	0.74	0.60	0.92	87	0.81	0.64	1.02	60	0.77	0.58	1.03	50	0.86	0.63	1.18

S Figure :Cut-off points for categories of alcohol consumption by study included in the meta-analysis



Green = alcohol consumption category defined as moderate for the purpose of the meta-analysis in which "moderate drinkers" were compared to non-drinkers.

Reference List

(1) Dite GS, Jenkins MA, Southey MC, Hocking JS, Giles GG, McCredie MR et al. Familial risks, early-onset breast cancer, and BRCA1 and BRCA2 germline mutations. J Natl Cancer Inst 2003;95(6):448-457.

(2) Cruz GI, Martinez ME, Natarajan L, Wertheim BC, Gago-Dominguez M, Bondy M et al. Hypothesized role of pregnancy hormones on HER2+ breast tumor development. Breast Cancer Res Treat 2013;137(1):237-246.

(3) Redondo CM, Gago-Dominguez M, Ponte SM, Castelo ME, Jiang X, Garcia AA et al. Breast feeding, parity and breast cancer subtypes in a Spanish cohort. PLoS One 2012;7(7):e40543.

(4) Bojesen SE, Tybjaerg-Hansen A, Axelsson CK, Nordestgaard BG. No association of breast cancer risk with integrin beta3 (ITGB3) Leu33Pro genotype. Br J Cancer 2005;93(1):167-171.

(5) Weischer M, Bojesen SE, Tybjaerg-Hansen A, Axelsson CK, Nordestgaard BG. Increased risk of breast cancer associated with CHEK2*1100delC. J Clin Oncol 2007;25(1):57-63.

(6) Chang-Claude J, Eby N, Kiechle M, Bastert G, Becher H. Breastfeeding and breast cancer risk by age 50 among women in Germany. Cancer Causes Control 2000;11(8):687-695.

(7) Fagerholm R, Hofstetter B, Tommiska J, Aaltonen K, Vrtel R, Syrjakoski K et al. NAD(P)H:quinone oxidoreductase 1 NQO1*2 genotype (P187S) is a strong prognostic and predictive factor in breast cancer. Nat Genet 2008;40(7):844-853.

(8) Kilpivaara O, Bartkova J, Eerola H, Syrjakoski K, Vahteristo P, Lukas J et al. Correlation of CHEK2 protein expression and c.1100delC mutation status with tumor characteristics among unselected breast cancer patients. Int J Cancer 2005;113(4):575-580.

(9) Syrjakoski K, Vahteristo P, Eerola H, Tamminen A, Kivinummi K, Sarantaus L et al. Population-based study of BRCA1 and BRCA2 mutations in 1035 unselected Finnish breast cancer patients. J Natl Cancer Inst 2000;92(18):1529-1531.

(10) Kawase T, Matsuo K, Suzuki T, Hiraki A, Watanabe M, Iwata H et al. FGFR2 intronic polymorphisms interact with reproductive risk factors of breast cancer: results of a case control study in Japan. Int J Cancer 2009;125(8):1946-1952.

(11) John EM, Hopper JL, Beck JC, Knight JA, Neuhausen SL, Senie RT et al. The Breast Cancer Family Registry: an infrastructure for cooperative multinational, interdisciplinary and translational studies of the genetic epidemiology of breast cancer. Breast Cancer Res 2004;6(4):R375-R389.

(12) Garcia-Closas M, Egan KM, Newcomb PA, Brinton LA, Titus-Ernstoff L, Chanock S et al. Polymorphisms in DNA double-strand break repair genes and risk of breast cancer: two population-based studies in USA and Poland, and meta-analyses. Hum Genet 2006;119(4):376-388.

(13) Anton-Culver H, Cohen PF, Gildea ME, Ziogas A. Characteristics of BRCA1 mutations in a population-based case series of breast and ovarian cancer. Eur J Cancer 2000;36(10):1200-1208.

(14) Ziogas A, Gildea M, Cohen P, Bringman D, Taylor TH, Seminara D et al. Cancer risk estimates for family members of a population-based family registry for breast and ovarian cancer. Cancer Epidemiol Biomarkers Prev 2000;9(1):103-111.