Supplemental Materials

Genome-wide interaction analysis of menopausal hormone therapy use and breast cancer risk among 62,370 women

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Table S1. Demographics characteristics of postmenopausal women in participating studies

Study	Study Design	Cases				Controls			
		N	Age, Mean	Current MHT use	Current EPT use	N	Age, Mean (SD)	Current MHT use	Current EPT use
CBCS	Population-based case-control	379	63.6 (8.1)	0.15	0.06	506	62.8 (8.1)	0.16	0.08
CECILE	Population-based case-control	519	61.2 (7.2)	0.17	0.13	604	61.2 (7.3)	0.14	0.11
CPSII	Prospective cohort	2,362	62.5 (5.8)	0.44	0.20	3,113	62.3 (5.9)	0.39	0.12
EPIC	Prospective cohort	1,680	59.0 (5.5)	0.31	0.26	1,766	58.7 (5.4)	0.31	0.23
GENICA	Population-based case-control	691	62.6 (8.6)	0.27	0.13	533	62.7 (8.7)	0.30	0.12
KARMA	Prospective cohort	836	64.6 (6.7)	0.10	NA	4,153	63.9 (6.2)	0.05	NA
MARIE	Population-based case-control	1,483	63.8 (5.5)	0.44	0.28	1,850	62.7 (5.5)	0.35	0.21
MCBCS	Mixed	973	63.3 (10.2)	0.19	0.19	981	62.1 (9.8)	0.25	0.14
MCCS	Prospective cohort	794	66.6 (8.5)	0.22	NA	874	65.5 (8.1)	0.17	NA
MEC	Prospective cohort	591	64.4 (8.6)	0.59	0.35	618	64.8 (7.7)	0.47	0.21
MISS	Prospective cohort	217	58.4 (6.0)	0.27	NA	591	57.1 (5.2)	0.18	NA
MMHS	Prospective cohort	216	64.6 (8.8)	0.25	0.07	460	63.3 (10.9)	0.28	0.05
NCBCS	Population-based case-control	1,075	60.0 (9.1)	0.25	0.10	596	59.9 (9.0)	0.44	0.15
NHS	Prospective cohort	890	66.6 (8.0)	0.40	0.18	1,513	67.6 (8.4)	0.28	0.10
NHS2	Prospective cohort	508	54.7 (4.4)	0.39	0.23	770	52.7 (5.0)	0.45	0.15
OFBCR	Mixed	666	58.5 (8.2)	0.32	NA	287	57.3 (6.4)	0.52	NA
PBCS	Population-based case-control	1,276	59.9 (8.3)	0.12	0.11	1,390	60.5 (7.4)	0.07	0.05
PKARMA	Mixed	2,320	65.4 (8.3)	0.18	0.05	2,463	60.4 (6.8)	0.08	0.02
PLCO	Prospective cohort	1,819	68.3 (6.4)	0.60	NA	2,578	62.3 (5.2)	0.56	NA
PROCAS	Population-based case-control	244	62.1 (5.4)	0.07	0.04	1,265	61.8 (5.9)	0.07	0.03
SASBAC	Population-based case-control	1,155	63.4 (6.4)	0.37	0.20	1,363	63.3 (6.3)	0.32	0.13
SMC	Prospective cohort	805	61.1 (7.7)	0.27	NA	520	60.8 (7.8)	0.45	NA
UCIBCS	Mixed	259	66.9 (9.7)	0.23	0.07	165	62.6 (7.3)	0.42	0.11
UKBGS	Prospective cohort	648	60.4 (6.9)	0.25	NA	626	60.3 (6.9)	0.17	NA
USRT	Mixed	304	64.1 (8.3)	0.50	NA	639	64.2 (8.5)	0.46	NA
WHI	Prospective cohort	4,875	69.0 (7.4)	0.44	0.25	4,561	69.3 (7.4)	0.36	0.18
Total		**27,585**	**64.0 (8.2)**	**0.34**	**0.19**	**34,785**	**63.0 (7.7)**	**0.28**	**0.13**

* CBCS: Canadian Breast Cancer Study; CECILE CECILE Breast Cancer Study; CPSII: Cancer Prevention Study-II Nutrition Cohort; EPIC: European Prospective Investigation Into Cancer and Nutrition; GENICA: Gene Environment Interaction and Breast Cancer in Germany; KARMA: Karolinska Mammography Project for Risk Prediction of Breast Cancer -

Cohort Study; MARIE: Mammary Carcinoma Risk Factor Investigation; MCBCS: Mayo Clinic Breast Cancer Study; MCCS: Melbourne Collaborative Cohort Study; MEC: Multiethnic Cohort; MISS: Melanoma Inquiry of Southern Sweden; MMHS: Mayo Mammography Health Study; NCBCS: North Carolina Breast Cancer Study; NHS: Nurses' Health Study; NHS2: Nurses' Health Study 2; OFBCR: Ontario Familial Breast Cancer Registry; PBCS: NCI Polish Breast Cancer Study; PKARMA: Karolinska Mammography Project for Risk Prediction of Breast Cancer - Case-Control Study; PLCO: The Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial; PROCAS: Predicting the Risk Of Cancer At Screening Study; SASBAC: Singapore and Sweden Breast Cancer Study; SMC: Swedish Mammography Cohort; UCIBCS: UCI Breast Cancer Study; UKBGS: UK Breakthrough Generations Study; USRT: US Radiologic Technologists Study; WHI: Women's Health Initiative Observational Study.
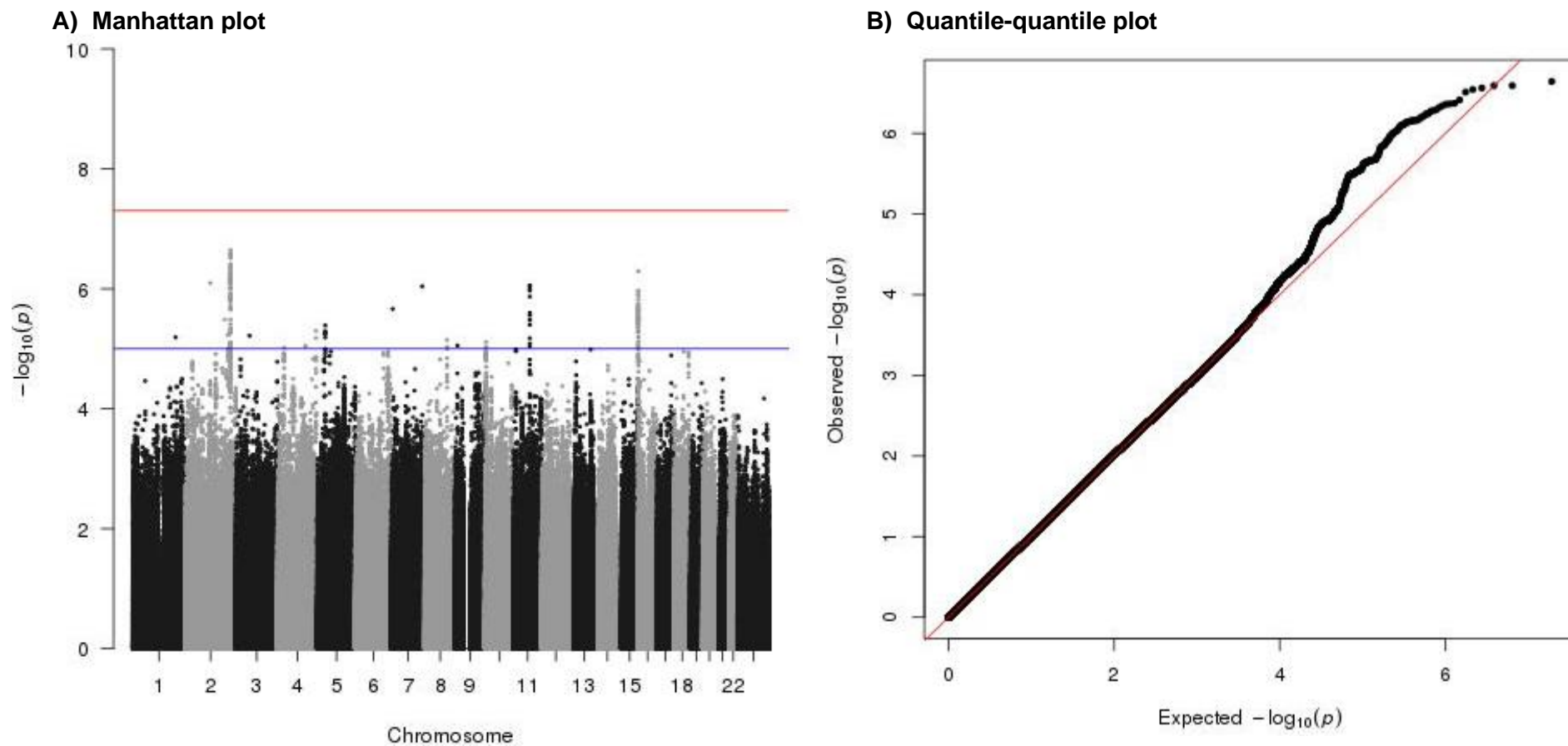
** Current MHT use: Current use of menopausal hormone therapy; Current EPT use: Current use of estrogen + progesterone menopausal hormone therapy

Figure S1. Manhattan plot and quantile-quantile plot of genome-wide interaction of current use of menopausal hormone therapy on breast cancer risk among population-based studies only
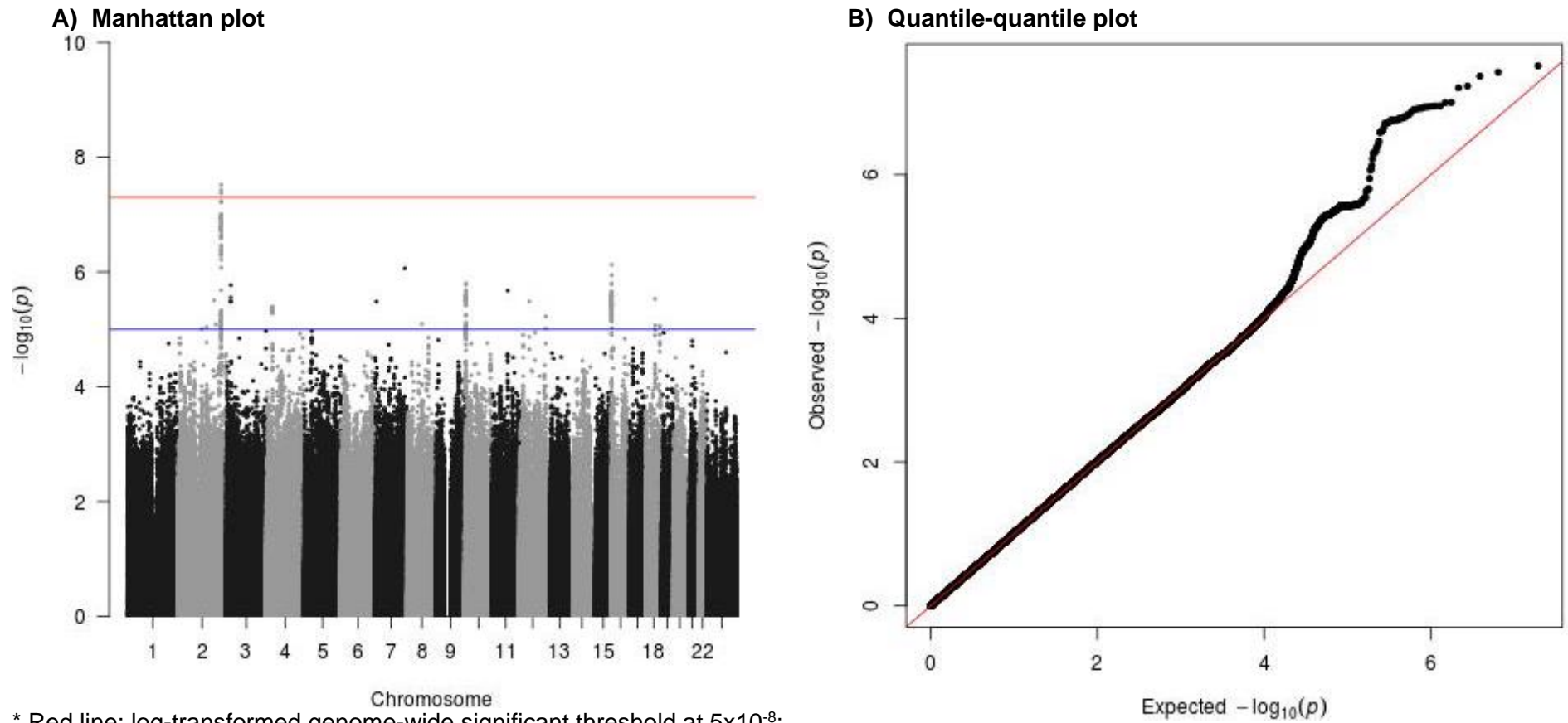
A) Manhattan plot

Chromosome

B) Quantile-quantile plot

Expected $-\log_{10}(p)$

* Red line: log-transformed genome-wide significant threshold at 5×10^{-8};
  Blue line: log-transformed suggestive threshold at 1×10^{-5}.

Figure S2. Manhattan plot and quantile-quantile plot of genome-wide interaction of current use of menopausal hormone therapy on estrogen-receptor positive breast cancer risk

A) Manhattan plot

B) Quantile-quantile plot

* Red line: log-transformed genome-wide significant threshold at 5×10^{-8};
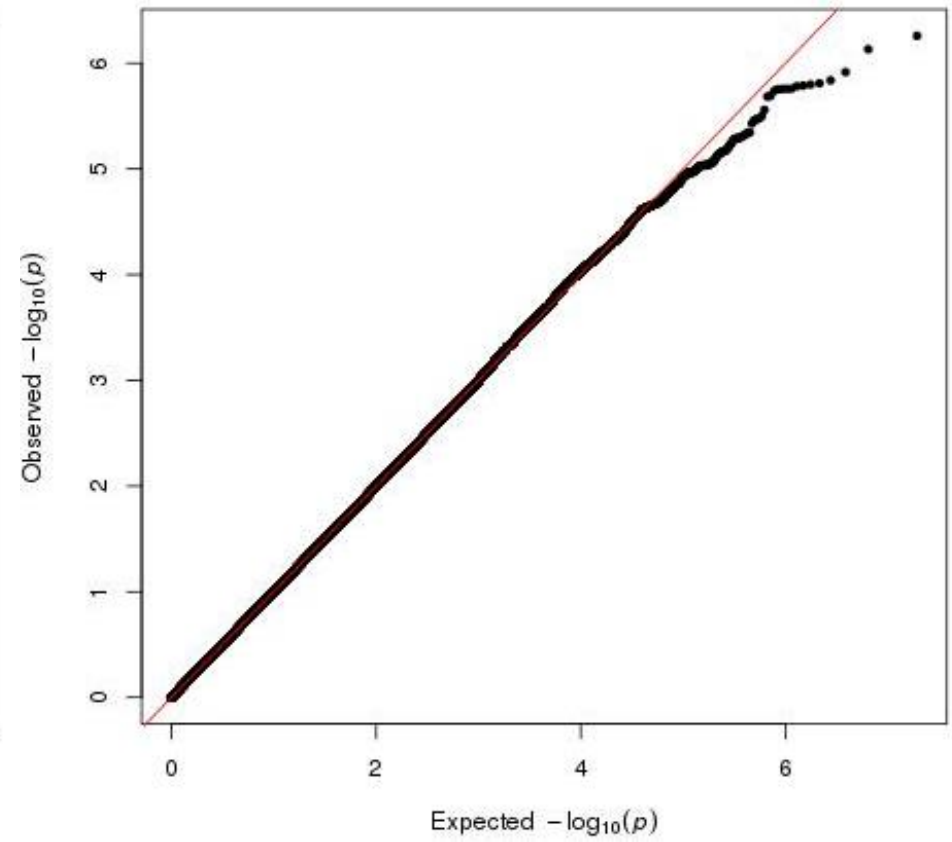 Blue line: log-transformed suggestive threshold at 1×10^{-5}.

Figure S3. Quantile-quantile plots of genome-wide interaction of current use of menopausal hormone therapy on breast cancer risk

A) Current MHT use
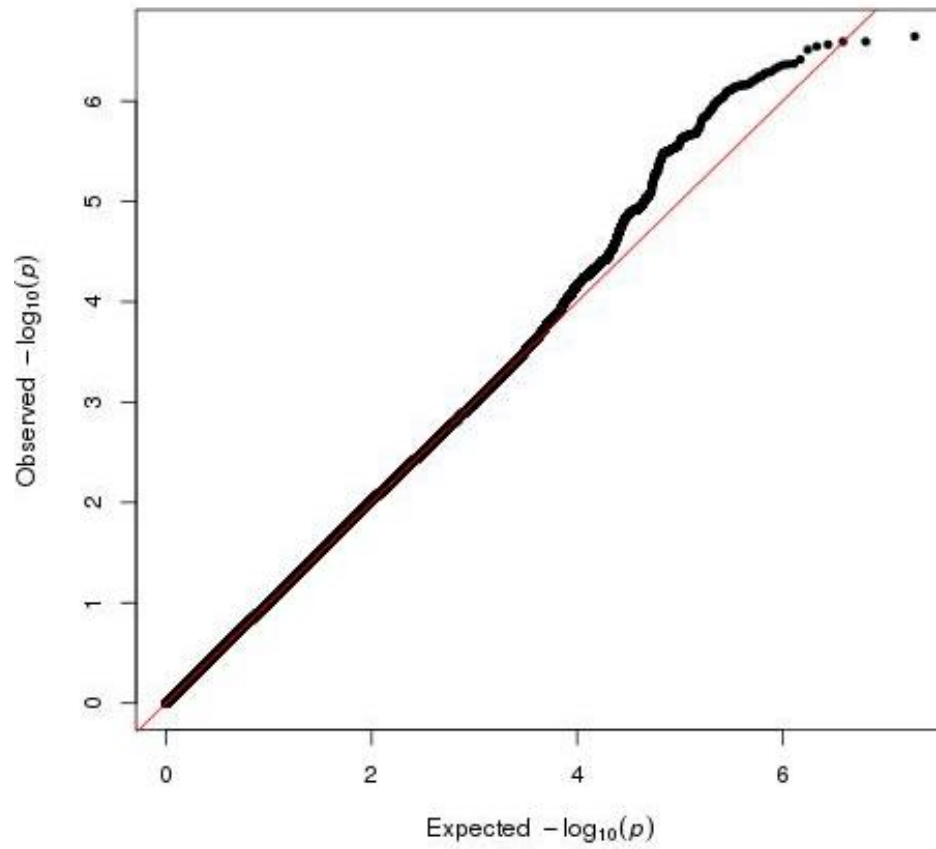
B) Current EPT use

* Genomic control factor λ=1.012

* Genomic control factor λ=1.006