**Supplemental Materials**

**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**

|  |  |
| --- | --- |
| 1. **Manhattan plot**
 | 1. **Quantile-quantile plot**
 |
| \* Red line: log-transformed genome-wide significant threshold at 5x10-8;  Blue line: log-transformed suggestive threshold at 1x10-5. |  |

**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**

|  |  |
| --- | --- |
| 1. **Manhattan plot**
 | 1. **Quantile-quantile plot**
 |
| A close up of a device  Description automatically generated\* Red line: log-transformed genome-wide significant threshold at 5x10-8;  Blue line: log-transformed suggestive threshold at 1x10-5. | **A close up of a map  Description automatically generated** |

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

|  |  |
| --- | --- |
| 1. **Current MHT use**
 | 1. **Current EPT use**
 |
| A close up of a map  Description automatically generated |  |
| \* Genomic control factor λ=1.012 | \* Genomic control factor λ=1.006 |