Supplementary Table 2. Univariate estimates of additive genetic (A), shared environment (C), and individual/non-shared environment (E) components mammographic density at baseline, mammographic density change/year, number of clusters of microcalcifications at baseline, and number of masses at baseline among sisters in the KARMA cohort (N=3,880). Estimates with 95% confidence intervals presented. Re-randomisation of siblings for all analyses due to issues with paternal half siblings having differing variances for the outcome ‘mammographic density change’

|  |  |  |
| --- | --- | --- |
|  | **Additive genetic**  **(A)** | **Individual/non-shared environment**  **(E)** |
| *(log) Mammographic density (cm2)a* |  |  |
| Unadjusted | 0.65 (0.57 to 0.74) | 0.35 (0.26 to 0.43) |
| Model 1 – age at mammogram, menopausal status, BMI | 0.55 (0.46 to 0.64) | 0.45 (0.36 to 0.54) |
| Model 2 –age at mammogram, menopausal status, BMI, HRT use, previous benign breast disorder, reproductive history | 0.58 (0.49 to 0.68) | 0.42 (0.32 to 0.51) |
|  |  |  |
| *Mammographic density change (cm2)/yeara* |  |  |
| Unadjusted | 0.01 (-0.09 to 0.10) | 0.99 (0.90 to 1.09) |
| Model 1 – age at first mammogram, menopausal status, BMI, age at last mammogram | 0.00 (0.00 to 0.00) | 1.00 (1.00 to 1.00) |
| Model 2 – age at first mammogram, menopausal status, BMI, age at last mammogram, reproductive history | 0.01 (-0.08 to 0.11) | 0.99 (0.89 to 1.08) |
|  |  |  |
| *Microcalcificationsb* |  |  |
| Unadjusted | 0.43 (0.24 to 0.61) | 0.57 (0.39 to 0.76) |
| Model 1 – age at mammogram, menopausal status, BMI | 0.25 (0.06 to 0.44) | 0.75 (0.56 to 0.94) |
| Model 2 –age at mammogram, menopausal status, BMI, HRT use, previous benign breast disorder, reproductive history | 0.24 (0.03 to 0.45) | 0.76 (0.55 to 0.97) |
|  |  |  |
| *Massesa* |  |  |
| Unadjusted | 0.14 (0.03 to 0.25) | 0.86 (0.75 to 0.97) |
| Model 1 – age at mammogram, menopausal status, BMI | 0.12 (0.01 to 0.24) | 0.88 (0.76 to 0.99) |
| Model 2 –age at mammogram, menopausal status, BMI, HRT use, previous benign breast disorder, reproductive history | 0.13 (0.01 to 0.25) | 0.87 (0.75 to 0.99) |

a the AE model was the best fit for the data bthe ACE model was the best fit for the data

Wald standard errors and confidence intervals were used, allowing confidence bounds of variances to be lower than zero.