Supplementary Table 1. Model fitting from univariate analyses of baseline information on 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). Re-randomisation of siblings for all analyses due to issues with paternal half siblings having differing variances for the outcome ‘mammographic density change’

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **AIC** | **-2LL** | **Diff-df** | **Diff-LL** | **p-value\*** |
| *(log) Mammographic density (cm2)*  |  |  |  |  |  |
|  Saturated Model | 4653.13 | 12197.13 | NA | NA | NA |
|  ADE | 4646.09 | 12212.09 | 11 | 14.96 | 0.184 |
|  ACE | 4648.19 | 12214.19 | 11 | 17.06 | 0.106 |
|  AE | 4646.42 | 12214.42 | 12 | 17.29 | 0.139 |
|  Model 1a | 3515.06 | 10697.06 | NA | NA | NA |
|  ADE | 3505.46 | 10709.46 | 11 | 12.39 | 0.334 |
|  ACE | 3504.59 | 10708.59 | 11 | 11.53 | 0.399 |
|  **AEe** | 3503.68 | 10709.68 | 12 | 12.62 | 0.397 |
|  Model 2b | 2891.67 |  9061.67 | NA | NA | NA |
|  ADE | 2886.41 |  9078.41 | 11 | 16.73 | 0.116 |
|  ACE | 2884.98 |  9076.98 | 11 | 15.31 | 0.169 |
|  **AEe** | 2884.51 |  9078.51 | 12 | 16.84 | 0.156 |
|  |  |  |  |  |  |
| *Mammographic density change (cm2) /year* |  |  |  |  |  |
|  Saturated Model | 12010.79 | 19344.79 | NA | NA | NA |
|  ADE | 12022.95 | 19378.95 | 11 | 34.16 | 0.0003 |
|  ACE | 12022.96 | 19378.96 | 11 | 34.17 | 0.0003 |
|  AE | 12020.97 | 19378.97 | 12 | 34.18 | 0.0006 |
|  Model 1c | 11370.78 | 18322.78 | NA | NA | NA |
|  ADE | 11384.15 | 18358.15 | 11 | 35.37 | 0.0002 |
|  ACE | 11384.15 | 18358.15 | 11 | 35.37 | 0.0002 |
|  **AEe** | 11382.15 | 18358.15 | 12 | 35.37 | 0.0004 |
|  Model 2d |  9799.22 | 15771.21 | NA | NA | NA |
|  ADE |  9825.63 | 15819.63 | 11 | 48.41 | <0.0001 |
|  ACE |  9825.61 | 15819.61 | 11 | 48.39 | <0.0001 |
|  **AEe** |  9823.64 | 15819.64 | 12 | 48.42 | <0.0001 |
|  |  |  |  |  |  |
| *Microcalcifications*  |  |  |  |  |  |
|  Saturated Model | -2800.37 | 4887.63 | NA | NA | NA |
|  ADE | -2754.12 | 4965.88 | 16 | 78.25 | <0.0001 |
|  ACE | -2754.12 | 4965.88 | 16 | 78.25 | <0.0001 |
|  AE | -2754.12 | 4965.88 | 17 | 78.25 | <0.0001 |
|  Model 1a | -2916.99 | 4433.01 | NA | NA | NA |
|  ADE | -2926.98 | 4455.02 | 16 | 22.02 | 0.143 |
|  ACE | -2926.98 | 4455.02 | 16 | 22.02 | 0.143 |
|  **AEe** | -2928.98 | 4455.02 | 17 | 22.02 | 0.184 |
|  Model 2b | -2480.79 | 3829.21 | NA | NA | NA |
|  ADE | -2492.43 | 3849.57 | 16 | 20.36 | 0.204 |
|  ACE | -2492.43 | 3849.57 | 16 | 20.36 | 0.204 |
|  **AEe** | -2494.43 | 3849.57 | 17 | 20.36 | 0.256 |
|  |  |  |  |  |  |
| *Masses*  |  |  |  |  |  |
|  Saturated Model | 2454.58 | 10142.58 | NA | NA | NA |
|  ADE | 2432.02 | 10152.02 | 11 | 9.44 | 0.894 |
|  ACE | 2431.57 | 10151.57 | 11 | 8.99 | 0.914 |
|  AE | 2430.02 | 10152.02 | 12 | 9.44 | 0.925 |
|  Model 1a | 2256.78 |  9742.75 | NA | NA | NA |
|  ADE | 2230.67 |  9748.67 | 16 | 5.92 | 0.989 |
|  ACE | 2230.17 |  9748.18 | 16 | 5.42 | 0.993 |
|  **AEe** | 2228.67 |  9748.67 | 17 | 5.92 | 0.993 |
|  Model 2b | 1965.69 |  8407.69 | NA | NA | NA |
|  ADE | 1939.77 |  8413.77 | 16 | 6.07 | 0.987 |
|  ACE | 1939.13 |  8413.13 | 16 | 5.44 | 0.993 |
|  **AEe** | 1937.77 |  8413.77 | 17 | 6.07 | 0.992 |

AIC- Akaike’s information criteris; -2LL – minus 2 log-likelihood; Diff-df – difference in degrees of freedom; Diff-LL – difference in log-likelihood; p-value – testing whether each model if statistically significantly different from the saturated model

A- additive genetic factors; D – dominant genetic; C- shared environment; E - non-shared environmental factors

\* p-value to test whether the nested model fits the data worse than the saturated model (p <0.05 indicates a poorer fit)

a adjusted for: age at mammogram, menopausal status, BMI

b adjusted for: age at mammogram, menopausal status, BMI, hormone replacement therapy use, previous benign breast disorder, and reproductive history (parity x age at first birth)

c adjusted for: age at first mammogram, menopausal status, BMI, and age at last mammogram

d adjusted for: age at first mammogram, menopausal status, BMI, age at last mammogram, hormone replacement therapy use, previous benign breast disorder, and reproductive history (parity x age at first birth)

e The AE model was preferred, given that it has fewer parameters and did not fit the data statistically significantly worse than the ACE model (result not shown)